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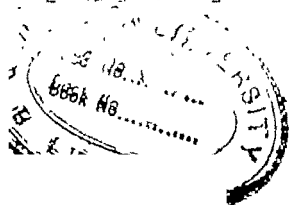
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STUDY OF THOMSEN'S DISEASE, BASED ON EIGHT CASES, IN A FAMILY EXHIBITING REMARKABLE HERITANCE FEATURES IN THREE GENERATIONS.

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rich literature on inherited abnormality of the neuro-muscular system is notably poor in information regarding the definite physical characteristics that might be regularly associated with a given abnormality in an affected family. The human race is too heterogeneous in numbers, too widely dispersed and too widely dispersed to permit of any generalizations regarding the linkage of certain physical characteristics with certain constitutional abnormalities. Lombroso's inference that the laws of heredity are too far-reaching, at a time when the working out of the laws was not good, to say the least.

value of accumulating information regarding the association of gross appearances of persons with certain conditions, is obvious. Certainly five, and of the eight observed in the present instance, if it were not for the

genita with the psychoses. In the first generation of the family described, the two disorders indeed co-exist in the same persons; in the second generation there is a clear-cut segregation of the disorders, each becoming associated with a definite physical person; three individuals of a certain type become affected with Thomsen's disease, and the other three, of a different physical type, become affected with psychoses. In the third generation the psychoses as well as the physical type associated with it, are eliminated. Four types appear, each represented by one individual who has inherited from a respective parent, not a blood-relation of the affected, that parent's physical type and normal constitution. The remaining members of the third generation are all of the myotonic type of the second generation, and they are all, with the possible exception of one who has not been studied, affected with myotonia.

The Mendelian phases of the family to be described may throw some light upon some of the pathological features of Thomsen's disease—the large musculature usually associated with it, and the muscular wasting which is sometimes observed.

Aside from the Mendelian phases, the cases in question have some interesting features, each of which has been described by Pelletier. Of two brothers examined by this investigator, one was affected with a very pronounced Thomsen's disease. The other had no symptoms of myotonia, although the presence of the disorder was maintained in him by the characteristic myotonic reaction. Of the nine cases in the family, five have to this day suffered no discomfort from the disorder; they are almost certain to die to their postnatal degeneration.

Finally, the cases are interesting in themselves. One of the features of the disorder, which has greatly facilitated the study of the mechanism

her minute or two, and she was quite normal again. Ever since then she has been subject to such attacks whenever suddenly excited or surprised. The writer witnessed one of these attacks in the patient's house. It occurred when an attempt was made to test the electrical reactions of her hands under rather disagreeable circumstances. On previous occasions the clinical and electrical tests had given negative results. On one such occasion an ice-pack was applied to one of her upper limbs in order to ascertain whether the chilling of the extremity would have the effect of manifesting the reflex reaction. Mechanical stimulation produced indeed weakly positive



A B C D

FIG. 1

On the occasion of the visit to the laboratory to test the electrical reactions under the influence of the upper limb with ice, it was carried out in the presence of the patient's mother, and she was rather disgusted by the application of the faradic current. A wave of the current was applied at the wrist, and the patient's neck and head were covered with a crown

very "nervous" woman all her life. She is subject to attacks of profound depression, alternating with states of irritability just like mother." She has, besides, attacks during which her lower limbs are cold and numb, especially at night, irrespective of the surrounding temperature. She has never had any muscular trouble.

Electrical and mechanical tests of her muscles gave negative results.

The second member of this group is William L. Junr., aged 36. Weight 145 lb.; carpenter by trade. In appearance he is very much like his sister Laura —, of medium stature and build, with a fair olive complexion, dark-chestnut-coloured hair and deep blue eyes. He married twice and has two children, one by each wife.

Two or three times a year William has attacks of "nervousness" of about two weeks' duration. During these attacks he goes "out of his mind"—does not work, wanders about aimlessly, and talks "go" and quite incoherently, repeating the same sentences over and over again. During a recent attack he appeared at his sister Louise's house at a distance of about five miles—at 3 o'clock in the morning. He shows no tendency to commit violence during these periods of disorientation. In the intervals he is a good, steady workman and a devoted husband and father.

He has never had any muscular trouble, and electrical and mechanical tests of his muscles revealed nothing abnormal.

The third member of this group is Harry L., aged 23. Weight 150 lb. Unmarried and a clerk by profession. In appearance he is like the two preceding members of this group, having the same colour of the skin, eyes and hair.

He suffers from "general nervousness," a general feeling of uneasiness in the presence of people, a sense of uneasiness. He is shy and awkward in all things. He has had headaches as long as he can remember. He has refused profitable employment for the last twelve months, being held back by some power for which he cannot account, and attempted suicide in a fit of despondency. "I strive for the higher things in life, but I cannot get a move on myself toward their attainment. I have no power. I cannot put myself forward. This makes me at all times down-beaten and at times despondent. I am just like mother used to be. You can tell by the way I speak the kind of a chap I am." One could indeed to a certain extent. His speech had a peculiarly slow quality, which appeared to be due not to any defect of the motor apparatus of speech, but to one of the mental processes corresponding to it. His responses were hesitant, as if from a general anxiety to say exactly the right thing while labouring under the conviction that he was about to say exactly the wrong thing.

He has never had any muscular trouble, and electrical and mechanical tests of his muscles showed them to be normal.

THE THIRD GENERATION.

This generation is represented by ten children, as follows:—

Herbert, of the myotonic group, has two children. Both resemble him in appearance, and the elder, who was examined for myotonia, was found to have it. The other was not examined.

Sarah E. M., of the myotonic group, has one child. In appearance this child resembles the father, who is not a blood-relation of the affected family, and he has neither muscular nor mental trouble.

Louise, of the same group, has five children. Four out of the five are of their mother's physical type and are affected by myotonia. The fifth, a girl, resembles her father, who is not a blood-relation of the family. Like her father, the girl is in every respect normal.

Laura and Harry, of the border-line psychosis group, have no children. William, of the same group, has two. They were not seen by the writer, but according to information furnished by the relations, the children look like their respective mothers—William having been married twice and each of his wives having given birth to one child. Like their mothers, who were not blood-relations of the family, the children have neither muscular nor mental trouble.

The third generation, then, falls into two groups: the normal and the myotonic. Of the five normal persons, two were examined, and one will suffice as an example. It is Estelle (fig. 1, E), the oldest child by the marriage of Louise and Frank W. She is 14 years of age, of a rather slender, athletic build. Like her father, the girl has a light olive complexion, green-blue eyes and red-brown hair, and presents neither muscular nor mental trouble.

The Myotonic Group.

Case 4.—Lorraine L., aged 7, is the elder daughter of Herbert L. She resembles her father in features, and in the colour of her skin, eyes and hair.

The child is well in every respect; her relations have not noticed any muscular abnormality.

Examination showed her movements to be normal. Mechanical and electrical stimulation of her muscles resulted in a normal contraction succeeded by a slow relaxation. The myotonic phenomenon was particularly marked in the right biceps and to a less degree in the other muscles of the same arm. The result of faradic stimulation was in this respect more definite than that of mechanical stimulation.

The tendon reflexes were normal.

In order to avoid repetition, the following may be said respecting the four cases of this group next to be described. All four, the children of Louise W., have certain physical characteristics in common. In appearance they all

resemble their mother, as may be partly judged from the family photograph (fig. 1), in their facial characteristics and in the colour of their skin, their eyes and their hair. The last, however, varies in shade according to age, the hair of the younger members being of a lighter shade than that of the older. The mother's hair is dark brown, while the children's hair varies from a golden brown in the older (Mildred), to a simple light brown in the youngest. The golden quality is said to be due to sunburn. Notwithstanding the difference in shade, however, the essential colour is the same in this group, and is distinctly different from that of the other groups. They all appear to have rather bulky muscles, but judgment in this respect becomes difficult when dealing with very young children.

Case 5.—Mildred W. (fig. 1, C), 12 years of age. She was the first of the series to present herself for examination. She was brought by her mother to the Neurological Division of the Vanderbilt Clinic on August 22, 1921, with the following history:—

The teachers of the public school which she attends complained to the parents that the girl, though sensible and obedient, behaved in a manner which introduced a certain amount of disorder into class discipline. She lacked the necessary promptness of action. She was the last to be on her feet when the order was given for the class to rise. She was the last to comply with the command of the teachers to put the pencils down on the desk, or to close the books. Ordered to recite, she was silent for a number of seconds; yet once she began, she proceeded smoothly. This initial retardation was especially evident in her physical exercises. A repeated command, or one uttered in an angry voice, made matters only worse. She retarded even more. Exhortation being of no avail, the teachers suspected a physical or mental defect and informed the parents.

The mother furnished the following data:—

Mildred is her second child. She was born at term, after a prolonged and difficult labour which was terminated, however, without the aid of forceps. The baby weighed 7 lb. at birth and appeared normal in every respect. She was breast-fed; cut her teeth at 7 months; said "papa" and "mamma" at 10 months and began to walk at 14 months. Her general health in childhood was very good. She had chicken-pox and measles and, at the age of 6, diphtheria without complications. She began to attend school at the age of 5, and she is at present in the 6th Grade, Grammar School, which is the normal grading for her age. She first menstruated a month ago.

Although the child began to walk at the normal period, it was soon noticed by the parents that she stumbled and fell a great deal. Later it was noted that she was reluctant to run about with the other children at play. Urging and scolding on this point having proven to be ineffective, the parents became reconciled to the condition.

Upon being questioned, Mildred stated that her tardiness at the beginning of movements is due neither to an inability to understand the meaning of a

command, nor to lack of desire on her part to fulfil it, but to a rigidity of the musculature involved, which supervenes the moment she attempts the particular movement. As a matter of fact the more anxious she is to carry out the movement promptly the greater is the rigidity which sets in, and the longer, therefore, is the retardation. Thus an angry or a repeated request on the part of the teacher, making her more anxious to comply, has exactly the opposite effect from that which is intended. Yet once the rigidity of the part wears off, she performs the movement without any difficulty. What is true of her movements in compliance with a command, is true also of the movements initiated of her own volition. She has much difficulty in ascending the first flight or two of stairs, but once she has climbed these she can climb the rest without any difficulty. While she is sitting in a chair, her muscles are perfectly lax, but the moment she attempts to rise they become rigid, and the rising movement is, therefore, executed clumsily. While she stands, she feels that her muscles are in a normal condition, but the moment she wishes to walk her muscles stiffen. After walking a few steps, however, the movements become normal. When she closes her eyelids tightly, she has difficulty in opening them for a number of seconds. If she presses her tongue against the palate, she feels it become rigid. The first movements of flexion and extension of the forearm at the elbow, with the hand relaxed, are a little difficult, but the succeeding movements are easy. But if she attempts to perform the same movements with the hand closed in a fist, flexion and extension of the forearm become more and more difficult, until after a few repetitions movement becomes impossible: the forearm remains semiflexed at the elbow, while the fingers half-open, and point in all sorts of directions in a grotesque manner from a contracted palm of the hand.

What is true of movements initiated of her own volition is likewise true of those which occur independently of her will. Thus, when she is suddenly and unexpectedly pushed from behind, she falls to the floor in a rigid mass. If she sneezes, her eyelids remain closed and she cannot open them for a time.

The girl is large, very muscular and powerful-looking. Weight 121 lb. All the subjective symptoms elicited on questioning were found to be true by objective examination, and need not be repeated. The peculiar behaviour of the movements of flexion and extension of the forearm upon the arm, which is apparently anomalous in Thomsen's disease, will be considered in the discussion as elucidating the mechanism of the abnormal muscular action. The reflex behaviour of the muscles was tested in several ways. The girl was made to sneeze (the administration of snuffing tobacco provided an excellent diagnostic agent) and her eyelids remained contracted for thirty seconds; during which she was making strenuous efforts to open them by the action of the frontalis muscle.

When a muscle was tapped with the percussion hammer, it contracted promptly and normally; the marked deviation from the normal being the slowness with which the muscle relaxed after the cessation of the stimulus. The degree of muscular contraction and the length of time taken by the

subsequent process of relaxation were in direct proportion to the strength of the blow and to the number of rapidly repeated blows. The table below gives the approximate number of seconds taken by the particular muscle or group of muscles to relax, after contracting in response to the stimulus of one, two and three moderate blows dealt in rapid succession with the percussion hammer.

	One blow	Two blows	Three blows
Right arm-biceps	10 seconds	5 seconds	20 seconds
Left arm-biceps	15 "	5 "	30 "
Right supinator longus	7 "	10 "	19 "
Left supinator longus	5 "	7 "	10 "
Right anterior forearm muscles	7 "	10 "	18 "
Left anterior forearm muscles	3 "	5 "	8 "
Right posterior forearm muscles	3 "	6 "	10 "
Left posterior forearm muscles	3 "	6 "	10 "
Right triceps	7 "	10 "	15 "
Left triceps	10 "	18 "	17 "
Pectorals	4 "	6 "	10 "
Sternomastoids	5 "	7 "	10 "
Posterior leg muscles	5 "	7 "	10 "
Peroneal muscles	5 "	7 "	10 "
Right thenar muscles	7 "	10 "	12 "
Left thenar muscles	7 "	10 "	12 "
Right hypothenar muscles	3 "	5 "	8 "
Left hypothenar muscles	3 "	5 "	8 "
Tongue	Not definite	8 "	5 "

The length of time taken by the muscles to relax after the cessation of the stimulus varied in a striking manner with the season of the year and the general condition of the patient's health. The table above held true for the moderately warm weather early in the autumn and a generally good state of the patient's health. With the onset of colder weather, and during slight indispositions, the relaxation time of the muscles was very much prolonged, in some instances doubled.

Stimulation with a faradic current of moderate strength produced the same effect as striking the muscles with a hammer, and the figures need not be repeated. Erb's classical reaction was not obtained in full.

What was true of a given number of blows of a certain strength was likewise true of a smaller number of blows of greater strength. Thus one strong blow produced the same effect as two or three gentler blows. And the same held good for faradic stimulation.

The superficial reflexes were normal. The radial, ulnar, wrist, supra-patellar and Achillis reflexes could not be obtained and a slight patellar reflex was obtained only with much difficulty.

The muscular strength, although good throughout, was not so great as one would expect considering the very large size of the muscles. Sensation was normal. The internal organs were apparently healthy. There was a trace of albumin in the urine, which was otherwise normal. The blood Wassermann test, done in order to exclude a possible complicating circumstance, was negative.

The patient was seen a number of times during the late summer, throughout autumn and the beginning of the winter. All the symptoms became exaggerated to an astonishing degree with the onset of cold weather. The movement of rising from a sitting position and the first steps were clumsy late in the summer. In the beginning of the winter she would rise from a sitting position with a sliding and turning movement, as if she had been glued to the chair; her first steps were made with the thighs and knees semiflexed, and it was not until she had walked for two or three minutes that her gait approximated the normal. She began to suffer with pains in her thighs and legs which were so severe that they interfered with sleep.

Case 6.—Edward W. (fig. 1, B), 10 years of age. His birth was difficult, but no instruments were used. Development normal. He had otitis media at the age of 6 months, measles at 2 years of age and pertussis immediately after. During the attack of pertussis circumcision was performed on account of some complication. At the age of 3 he developed diphtheria; antitoxin was administered, but post-diphtheritic paralysis of all four extremities occurred, lasting for nine weeks. Recovery was apparently complete.

The boy attends a public school and is quite bright at his studies. No symptoms of any muscular abnormality have been observed either by the family or by the teachers.

Upon examination the movements in response to commands were carried out normally, but mechanical and faradic stimulation of the muscles showed a persistence of the contraction after the cessation of the stimulus. The abnormality was particularly marked in the biceps, the supinator longus and the thenar muscles on both arms. Faradic stimulation was more effective in eliciting the abnormality than mechanical stimulation. The tendon reflexes were normal.

Case 7.—Mabel W. (fig. 1, F), aged 5. Instrumental delivery. Development normal. No diseases of childhood.

For some time it has been noticed that after the child sneezes her eyelids remain closed for a number of seconds, and that she remains hesitant when urged to perform a sudden movement. This is particularly marked when getting off a street car, just as in the case of her grandmother. On such occasions her legs remain "bound" for a time, so that she has to be supported or carried out.

Physical examination revealed the symptoms and signs of Thomsen's disease. When the child was asked to close and open her hand repeatedly each successive movement became more difficult, so that after a few movements the fingers remained extended upon the contracted palm, pointing in different directions. If she persisted, however, the difficulty was soon overcome, and the subsequent movements were normal. The following myogram (fig. 2) shows clearly the behaviour of the anterior muscles of the forearm in the attempt to open and close the hand repeatedly. Made to sneeze, the eyelids remained closed for a number of seconds.

Mechanical and faradic stimulation of the muscles revealed a persistence of the contraction beyond the time during which the stimulus was applied. The phenomenon was especially marked in the arm-biceps, the supinator longus, the muscles of the thenar and hypothenar eminences, and the calf muscles on both sides.

In every other respect the child appeared to be quite well and normal.

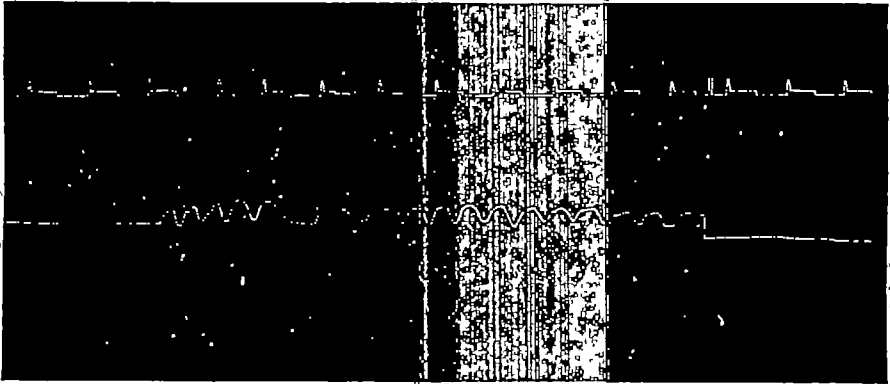


FIG. 2.—(Case 7.) Anterior forearm muscles in the attempt to open and close the hand repeatedly.

Case 8.—Nathalie W. (fig. 1, A), 3 years and 6 months of age. Instrumental delivery. Development normal. No symptoms of Thomsen's disease.

Gentle tapping with the percussion hammer and weak faradic stimulation gave indefinite results. Stronger stimulation was not practicable in the case of the young child. The administration of salt proved to be a valuable diagnostic measure; after sneezing, the entire eyelids remained tightly contracted for some seconds, and then opened very gradually in the course of ninety seconds, the orbicularis standing out with peculiar prominence. The tendon reflexes were normal.

THE MECHANISM OF THE ABNORMAL MUSCULAR ACTION.

This was studied to advantage in the movements of Mildred's (Case 5) upper limb.

With the hand and fingers relaxed the patient had some slight difficulty in going through the first few movements of flexion and extension of the forearm upon the arm. The first movement was quite normal, the second slightly difficult, the third, fourth, and fifth progressively more difficult, the sixth less difficult, the seventh still less so, the succeeding movements being normal. The myograms reproduced in figs. 3, A and 3, B were taken from the patient's biceps.

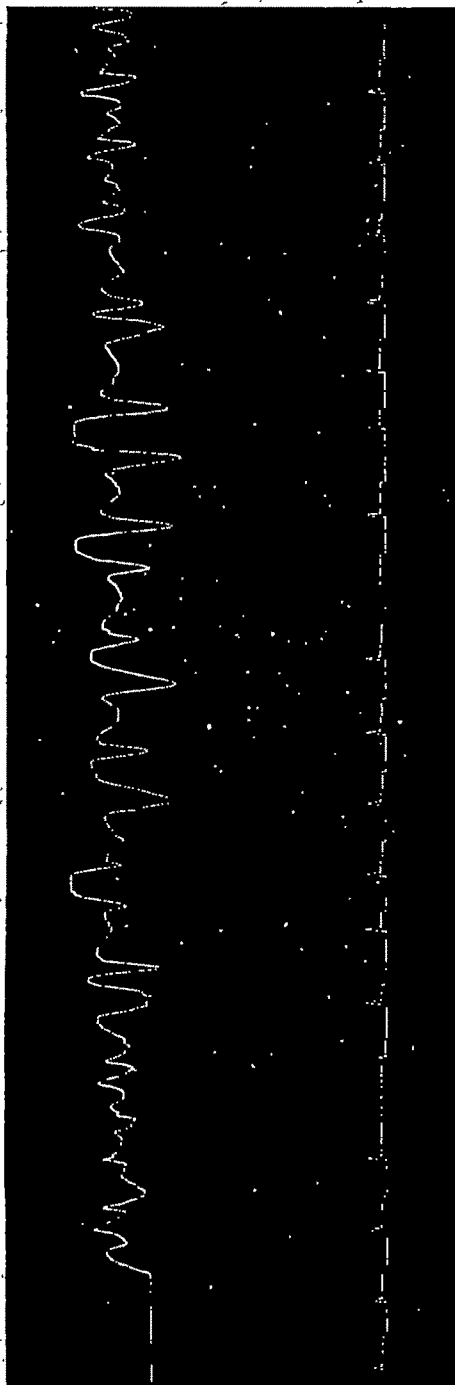


FIG. 3, A.—Mildred W. (Case 5). The behaviour of the biceps in the action of flexion and extension of the upper limb at the elbow with the hand relaxed.

When, however, flexion and extension of the forearm at the elbow were performed with the hand closed in a fist, the curve was never completed; the retardation increased until the movement ceased (fig. 3, B). Each succeeding movement was more and more difficult until after four or five repetitions the forearm remained semi-flexed upon the arm, the fingers being opened and extended in different directions upon a contracted palm. The entire musculature of the upper extremity was contracted, the individual muscles standing out prominently.

A somewhat similar instance has been described by Wichmann [44], who considered it "a fluke of Thomsen's disease." Martius and Hansemann [25] have observed an analogous phenomenon in a case of paramyotonia; and Pelz [32] cites a case of Weichmann's, in which a tonic spasm occurred after forced movement.

The seeming discrepancy of this phenomenon with the general tendency of the movements to be-

come normal after a few repetitions throws a good deal of light upon the mechanism of the muscular action in this disease. The facts in connection with this phenomenon will, therefore, be taken up in greater detail.

When the patient's arm biceps was gently tapped with the percussion hammer, the response by a contraction was quite normal. The subsequent relaxation, which in the case of normal muscles follows immediately after the momentary contraction, was in the case of the patient gradual, extending over a number of seconds. If, after the muscle was completely relaxed, it was tapped again, the same phenomenon was repeated. If, however, the muscle was tapped while

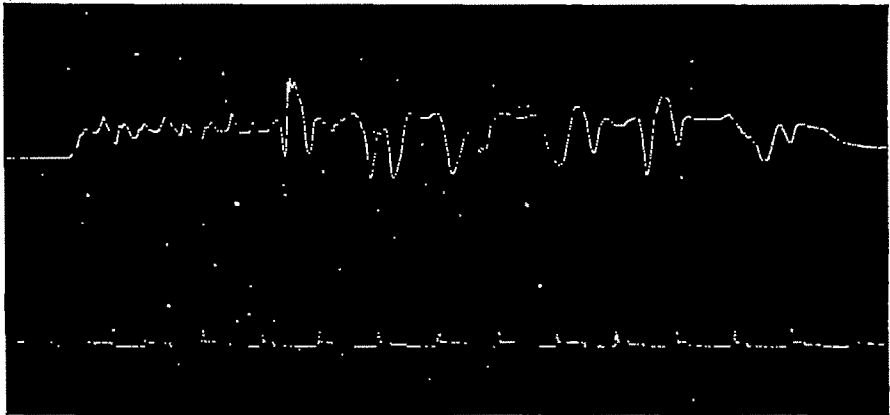


FIG. 3, B.—The same with the hand closed.

it was still contracted, the subsequent response was a seemingly greater contraction. By tapping the muscle, say six or eight times in rapid succession, it became contracted into an irregular, angular mass, of a woody consistency to the touch, and the patient complained of a pulling pain in the bicipital fossa. What happened was a simple summation of the preceding residual contractions. The succeeding relaxation then took a considerably longer time.

When the biceps and the triceps were alternately struck in rapid succession, the biceps did not contract into an irregular ball. After a few blows the forearm remained semiflexed upon the arm and the biceps muscle, although very firm to the touch, retained its regular belly-shape. This muscle was obviously held back from contracting into a ball by the persistent pulling of the opposing triceps.

It made no difference by what stimulus the action of the muscle was evoked, whether by tapping with a hammer, or by an electric current, or by volition or emotion, the resulting abnormal phenomenon was always the same—a persistence of the contraction beyond the duration of the stimulus and, in the case of a stimulus repeated in rapid succession, a simple summation of the residual contractions.

It is not an easy matter, however, to bring a volitional or an emotional stimulus to bear upon any single muscle, as may be done by the tap of a hammer, or the application of a faradic terminal. Unless the forearm is thoroughly supported, a request to contract the biceps, except in the case of a few especially gifted persons, will result inevitably in the contraction of a number of muscles, including some of the antagonists. For this there are two reasons. One is that in the habitual movement of flexion at the elbow, all the muscles passing over the anterior aspect of that joint take part. The other reason is that in order to enable the biceps to exert a measured pull upon the forearm the arm is fixed at the shoulder joint by all the muscles passing over that joint, including the antagonistic triceps.

We shall presently see how these facts furnish a clue to the entire mechanism of the abnormal muscular action in Thomsen's disease in all its varied aspects.

Let this be borne in mind that what is true of the necessity of fixing the shoulder joint in the movements of the forearm upon the arm, is true as well of the necessity of the fixation of any proximal part for the purpose of moving a distal segment to which it is immediately or mediately linked. Thus, in order to make a fist, the elbow and the shoulder joints must be fixed in any position of the upper extremity, except perhaps in the perpendicularly downward position. In order to move the upper part of the trunk, the muscles of the lower part of the trunk are contracted, thus converting a number of the lower vertebræ into a solid column from which the attached muscles can exert a pull upon the upper vertebræ. Since the larger muscles pass over more than one joint, it follows that the contraction of such a muscle may subserve two purposes simultaneously: one, the movement of the distal segment; the other, the fixation of the proximal segment.

When our myotonic patient is requested to make a fist and then to flex and extend the forearm upon the arm, she begins, therefore, these movements with the musculature of the upper extremity already in a state of partial contraction. When a normal person, under similar conditions, flexes the upper limb at the elbow, the extensors, contracted

for the purpose of fixing the forearm at the elbow and the arm at the shoulder, relax in correct proportion to the contraction of the flexors. In the myotonic person, however, the contracted extensors do not relax with sufficient despatch. The force exerted by the flexors in order to raise the mere weight of the forearm must be greater than normal by the amount necessary to overcome the pull of the opposing extensors. This is accomplished by sending a stronger volitional stimulus to the flexors, and the patient may be plainly seen to exert the volitional effort. The resulting greater contraction of the flexors, however, is succeeded by their slower relaxation. In the next succeeding movement of extension, the muscles engaged in that movement are called upon to work against the force of the tightly contracted flexors.

A succession of movements of flexion and extension, brought about by muscles which are already contracted for the purpose of fixing the segments of the limb (the hand being closed in a fist), results, therefore, in the myotonic person, in something more than a simple summation of the residual contractions. We have here a system of mutually aggravating conditions, and the residual contractions of the antagonistic groups of muscles are accumulated in a geometric ratio.

Thus, considering the manner in which the residual contractions are summated in the biceps and triceps in the alternate contractions of these muscles, the greater the amount of residual contraction of the triceps the greater must be the contraction of the biceps in order to move the forearm through a given angle. The subsequent residual contraction of the biceps is greater, therefore, in amount than it was in the case of the triceps. When the triceps is now called upon to extend the forearm, the amount of force which it must exert is greater than that exerted by the biceps in flexing it, and the subsequent residual contraction greater now than at the beginning. The amount of force which the biceps must exert in flexing the forearm the second time must, therefore, be greater than that exerted in flexing it the first time.

The result of the geometric summation of the residual contractions of opposing muscle groups, is that after a few movements of flexion and extension the entire musculature of the limb is contracted to its utmost capacity. Every segment then remains in a position between flexion and extension.

It is almost certain, however, that if the patient could overcome the rigidity and flex and extend the forearm a few more times, the succeeding movements would become easier and finally normal. This is

the case with every other movement of Mildred and with the same movement when performed by her sister Mabel (Case 7). What happens in the particular instance may be likened to the case of a traveller who, having climbed a hill, is so exhausted near its summit that he cannot surmount it and cannot, therefore, get to the other side where travelling is easy.

In view of our ignorance of the ultimate causes of muscle contraction, it would be useless to speculate upon the reasons for the diminution and the final disappearance of the residual contraction of the myotonic muscles upon the repetition of the movement in which they are engaged. Thomsen ascribed the abatement of the rigidity upon repetition of the movement to a concomitant rise in the temperature of the active muscle. Considering the effect of temperature upon chemical processes and upon the phenomena of osmosis and of surface tension, as well as the fact that all conditions of muscular rigidity are lessened under the influence of a higher temperature, Thomsen's assumption may not be far from the truth.

The mechanism of the rapidly accumulating residual contractions of opposing muscle-groups accounts for the sudden falling "like a log" of some myotonic patients under the influence of sudden strong psychic or emotional stimuli. Cases 2 and 5 are examples of such patients. Such instances have been described by Charles Bell [3] as early as 1837, before the disease was recognized as a definite entity. Thomsen speaks of the effect of psychic stimuli upon the myotonic person as follows: "When a psychic impression awakens the muscular cramp, whether it is fright . . . a friendly blow on the shoulder from behind, or when the foot strikes against an unexpected stone, or when a sudden noise reaches the ear, a painful feeling shoots through the entire voluntary musculature, like an electric current. Every affect is exaggerated in the susceptible disposition, fright and anger as well as joy."

The effect of a sudden strong psychic or emotional stimulus is to fix every proximal segment of the body and the limbs preparatory to any possibly desired movement of the distal segments. Throughout the vertebrate and a large part of the invertebrate kingdom, this fixation of the proximal body-segments may be observed in the act of "priming," which precedes the movements of aggression or escape. In man, under normal conditions, the widespread effect of a sudden strong emotional stimulus upon the general musculature of the body is little noticed: the general stiffening is usually of momentary duration; and where the duration is longer the rapidly alternating con-

tractions and relaxations of antagonistic muscles are exactly timed, constituting a perfectly co-ordinated system. Such is not the case in Thomsen's disease. In this disease there occurs, as we have seen, an overlapping of the contractions of alternately acting antagonistic muscles. In the rapid series of such alternating contractions of numerous antagonistic muscles which constitutes the act of "priming" there must occur, therefore, in the myotonic person a rapid accumulation of the residual contractions. The result of such an accumulation is that in a few moments the muscles become contracted to their utmost capacity and the person, no longer able to perform the fine balancing movements necessitated by the erect position, falls "like a log." In the instance of a similar attack described (Case 2), the parts of the patient which were thoroughly supported escaped rigidity. Since the muscles of these parts were not at work at the time, there was no basis for the formation of a series of mutually increasing residual contractions of antagonistic muscle-groups.

It will be remembered that the amount of *residual* contraction is in direct proportion to the degree of contraction; and that the degree of contraction is in direct proportion to the intensity of the stimulus. This explains the reason why in the instance of Case 1 the hand became "bound" only when the act of grasping was accompanied by that of lifting. The stronger stimulus determined to the muscles engaged in the double exertion of lifting and of grasping, made the myotonic condition of those muscles manifest where a weaker stimulus was inadequate.

The mechanism of mutually increasing *residual* contractions of antagonistic muscles differs essentially from Brissaud and Bauer's [6] explanation of the abnormal muscular action by a "synergic contraction of the antagonists." In the light of this mechanism, Jaquet's [18] theory of the irradiation of the nervous impulse to opposed muscle-groups is untenable. Johnson and Marshall's [20] idea of a block in the pyramidal system as the cause of the trouble is inconsistent with the symptomatology of the disease. From these authors' description it does not appear that they found in their cases either the sign of Babinski, or exaggerated deep reflexes, or abnormal associated movements, or a persistent hypertonus of the resting muscles, or any of the signs of interruption of the pyramidal path. Such signs have not indeed been mentioned by any writer as part of Thomsen's disease, notwithstanding the fact that Thomsen himself thought the disease to be due to a defect of volition. The intactness of the pyramidal

system in this disease is fully attested both by the absence of the signs just mentioned, and by the readiness with which a given set of muscles responds to the impulse of volition. Yet contract as it may, a muscle cannot move the part to which it is attached if that part is held back by an equivalent or by a greater force; and the retardation of movements in Thomsen's disease is not due to any tardiness of the muscles in contracting, but to the resistance offered by the unrelaxed antagonists.

Hoffmann [15] mentions a number of theories brought forward by different observers to explain the singular affection, and there is no need for repeating them here.

THE BEARING OF HEREDITY ON THE LARGE MUSCULATURE ASSOCIATED WITH THOMSEN'S DISEASE.

The distinctive features of the pathological state, as demonstrated by Jacoby [17], Schifferdecker [34], Dejerine and Sottas [8], Pelz [32], Johnson and Marshall [20] and others, are the great thickness of the fibres of the voluntary muscles, the great number of nuclei which are also found within the sarcoplasm and, in some cases, an increase of the interstitial tissue. Jacoby made the interesting statement that "it is obvious that a considerably larger number of embryonic sarcoplasts must have entered into the construction of each individual fibre than is the case in normal development."

It is certain that although Thomsen's disease does occur in persons with a musculature of average size, such an occurrence is quite exceptional. Assuming that the size appeared normal in the cases where no mention is made of it, the number of myotonics with muscles of ordinary bulk must still be quite small. By far the greater number of writers on Thomsen's disease speak of the large size of the musculature of the persons affected by it. Westphal [43] considered the disease to be "a singular congenital anomaly of muscle tone connected with an unusual increase of volume." Mills [26] tried to account for the large size of the muscles by "the frequently repeated, forced exercise."

A study of the family in question furnishes the following facts regarding the association of myotonia with a large musculature:—

The first male, who was not myotonic, had a large musculature; while the first female, who was myotonic, had muscles of the average normal size. Of their six surviving children, three have large and three average-sized muscles. Those with large muscles are myotonic,

while those with muscles of normal size are not. A glance at the respective weights of the six members of the second generation tells the story. The weights are as follows:—

Myotonic group				Non-myotonic group			
Sarah, aged 45,	weight	228	lb.	Laura, aged 41,	weight	156	lb.
Louise, „ 35,	„	228	„	William, „ 36,	„	145	„
Herbert, „ 38,	„	210	„	Harry, „ 23,	„	150	„

Of the ten members of the third generation, four have no myotonia and their musculature is of normal size; while five who are known to be myotonic show a tendency to a large musculature. Another shows the same tendency, but has not been examined for myotonia. In the case of the younger children, however, it is difficult to form a positive opinion as to the size of the muscles, and one judges largely from general impressions, which may a few years hence prove to have been wrong. But there is no doubt whatever in the case of the oldest myotonic member of the third generation, Mildred (fig. 1, C). She is 12 years of age, has very large muscles and weighs 121 lb.

With the exception, then, of the one child who has not been investigated, it may be said on the whole that those of the descendants who have inherited the first male's large musculature have also inherited the first female's myotonia; while those who have inherited the first female's average-sized musculature, have inherited the first male's normal muscular state.

The last feature assumes somewhat greater significance when the other inherited characters are considered together with the inheritance of the two characters just spoken of. The tabulated inherited characters are as follows: the muscular condition, the size of the muscles, the colour of the eyes, hair and skin, the form of the nose, the facial expression, the mental state and the sex. It must be understood at the outset, however, that conclusions respecting the colour of the eyes and hair drawn from ordinary observation, as was done in the present instance, are not entirely reliable. The writer was assured by so eminent an authority on Mendelism as Professor T. H. Morgan that, with the exception of the colour of the skin, exact colour determinations are made possible only by means of rather complicated tests. In estimating the colour of the hair, allowances must be made for the shade, which varies with age. Nothing has been said in the report of the cases about the form of the nose and the facial expression, because these characters are even more difficult to define with any degree of exactness than is the colour of the eyes and hair.

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The shape of the nose in the myotonic members of the family appears in several ways different from that in either the psychotic or the normal group. A single instance will suffice for illustration: the tip of the nose in these myotonic persons is pointed; in the three members of the psychotic group it is rounded. The four types of normal persons have as many different types of noses; Estelle's nose, for example, is of the "humped" variety, and exactly like her father's.

The expression of the face as a single hereditary entity is a good example of that conception of the Mendelian unit character which is so thoroughly condemned by Pearson [30], Conklin [7], Morgan [27], and other experts in Mendelism. A moment's thought must indeed make it plain to anybody that a great number of items, both structural and functional, conspire in the production of a given facial expression. The inheritance of that "unit character" must imply, therefore, the inheritance of all the numerous factors which constitute it.

It is the opinion of the older members of the affected family—and that opinion is largely upheld by photographs—that all the myotonic members have inherited the tip of the nose and the facial expression from the grandfather—the first male; and that the psychotic members have inherited these characteristics from the grandmother—the first female.

In the following table the particular form of the nose will be designated as pointed, rounded or humped; and the different facial expressions as A, B and C.

From this table we gather the following facts:—

(1) That with the exception of *myotonia* and *no myotonia*, the recorded characters of the first male, as well as those of the first female, formed an unbroken chain which was transmitted as a whole, constituting the general appearance and the mental state of the particular individual.

(2) That in some of the offspring the general appearance and the mental state of the first male, in others those of the first female, have proved to be dominant.

(3) That the offspring who have inherited from the first male his general appearance and his normal mental state, have also inherited from the first female the character of *myotonia*.

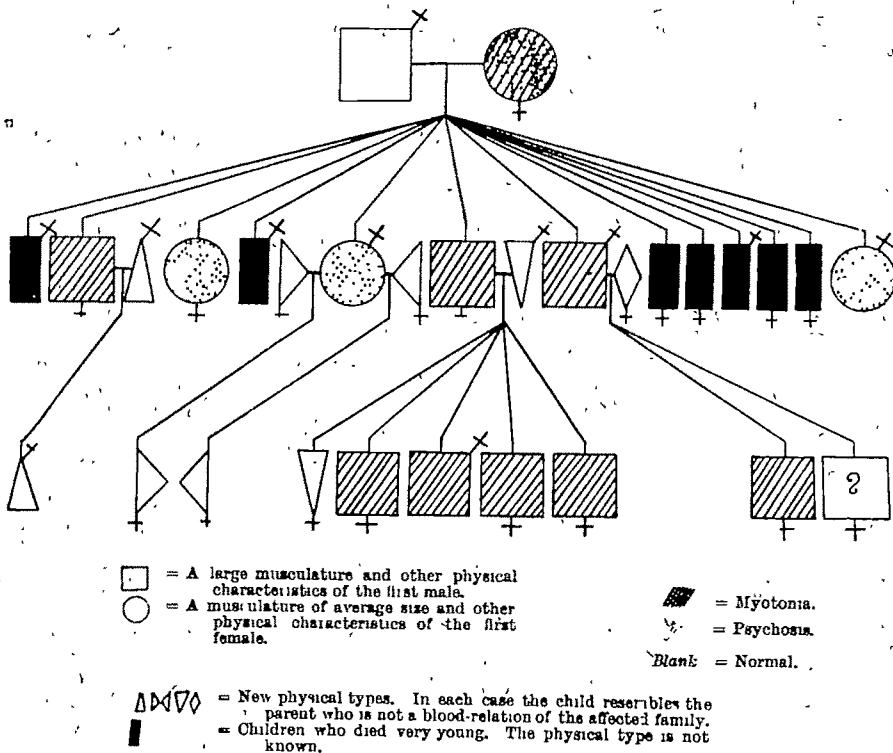
(4) That the offspring who have inherited the general appearance and the abnormal mental state of the first female, have also inherited from the first male the normal state of his musculature.

(5) That *myotonia* is not sex-linked in these cases.

No myotonia	Myotonia
Large muscles	Average muscles
Fair skin	Dark olive skin
Blue grey eyes	Deep blue eyes
Brown hair	Chestnut hair
Pointed nose	Rounded nose
Expression A	Expression B
No psychosis	Psychosis
Male	Female

3 An example of the four new types is that of the female at the extreme right. In appearance she is like her father (immediately above) who is not a blood-relation of the family.

The records on myotonia congenita make no mention of the association of any special physical characteristics with the muscular abnormality, with the exception of a large musculature. Since no general inference can be drawn from a single instance, we are for the present justified in the conclusion that *the particular character which offered a ready linkage to the character of myotonia, was that of a large musculature.*



Notes.—The arrangement is in the order of birth.

FIG. 4.

In the case of the family in question, then, it would appear that some of its members have a large musculature, not because they are myotonic, but because the hereditary factor of a large musculature proved to be a favourable receptor for the hereditary factor of myotonia.

ON THE QUESTION OF PARAMYOTONIA.

Eulenberg [11], Delprat [9], v. Sölder [39], Senator [38], Martius and Hansemann (25) and others, have described cases in which a tardy relaxation of the contracted muscles occurred only in the cold. In some of the cases of the first two authors the muscles remained contracted for long periods of time, in some instances for hours. Erb [10] was of the opinion that cases of this sort belonged to an entirely different category. The affection has received the name of paramyotonia. That there is hardly any justification for setting such cases aside in a different group from Thomsen's disease will appear from the following considerations:—

Quite a number of observers point out the fact that the manifestations of Thomsen's disease are much more apparent during the prevalence of cold weather. Kron [23] goes so far as to include the influence of cold in increasing the prominence of the symptoms among the points which justify a diagnosis of myotonia. In Case 2 of the present series, the myotonic reaction of certain muscles, which was not apparent under ordinary circumstances, was demonstrated after chilling the parts. In Case 5 the myotonic condition of the musculature is exaggerated in a most striking manner in cold weather and by slight general indispositions, such as the menstrual period or an ordinary coryza.

No two of the eight cases of the present series are of the same grade of severity, nor do any two exhibit quite the same manifestations of the affection. In one the tardy relaxation of the muscles occurs only when their contraction has been brought about by a primitive form of stimulus—the so-called emotional or psychic stimuli of fright or anger—and then the myotonic phenomena are most pronounced. In another, almost any stimulus capable of evoking a muscular contraction is sufficient to manifest the myotonic condition of the muscles. In still others only stimuli applied directly over the muscle bring the abnormality to light. The fact that in some of the cases classed under the heading of paramyotonia Erb's classical reaction could not be obtained, means only that a muscular contraction brought about by a stimulus applied from outside directly over the muscle was not sufficient to elicit the myotonic reaction of that muscle. It will be remembered that in Case 8 of the present series such stimuli were ineffective, while the contraction of the orbicularis palpebrarum brought about by the act of sneezing showed beyond a doubt the myotonic condition of that muscle.

Viewing the matter from this standpoint, one is no longer surprised to find that two members of the paramyotonic family described by

Delprat were affected with typical forms of Thomsen's disease. As is the case in every other disease, the manifestations of Thomsen's disease are somewhat different in different persons, and different in the same person under varying conditions. Yet for all its variations the main feature of the disease remains the same—an inherited affection characterized by the failure of the contracted muscles to relax with a sufficient degree of despatch.

MYOTONIA WITH MYATROPHY. A MENDELIAN SUB-LETHAL FACTOR.
MYOTONIA ACQUISITA.

The number of cases in which myotonia is associated with muscular atrophy is very considerable. Nearly all writers agree that the muscular strength of persons affected with Thomsen's disease, in relation to the size of their muscles, is below the normal. The coincidence of myotonia with gross muscular atrophy has been described by Hoffmann [14], Jolly [21], Schultze [37], Bettmann [4], Pelizaeus [31], Batten and Gibb [2], Nonné [29], Fuchs [13], Rossolimo [33], Lannois [24], Noguès and Sirol [28], v. Voss [42], Ramsey Hunt [16], and others. Pelz estimates the occurrence of atrophy in myotonia at 11 to 12 per cent. The fact that atrophied fibres have been found mingled among the greatly hypertrophied ones in cases where there was no gross muscular atrophy, is significant.

After observing the manner in which antagonistic muscles interfered with each other's actions, it occurred to the writer that atrophy might be caused by the repeated pulling and stretching—an actual tearing of muscle-fibres by the antagonistic muscles. The action of the facial muscles, however, would appear to be altogether too weak for such an accident to occur. Yet the facial muscles are involved in the atrophy in a great number of the cases described.

That some nerve elements are involved in the disease in a number of cases might easily be surmised from certain of the subsidiary symptoms. A number of these patients suffer with muscular pains. In the present series Cases 2, 3 and 5 complain of such pains. The diminution or the absence of some of the tendon reflexes is not infrequent in the more pronounced cases of myotonia without any atrophy, and it is very frequent in the cases with atrophy. In the most pronounced case of the present series, Case 5, most of the tendon reflexes are absent or very much diminished, yet there is no discoverable atrophy, and the muscles, when struck with the hammer, respond by normal contractions. The widespread and long-lasting paralysis caused by diphtheria in Cases 2

and 6 (at the ages of 18 and 3 respectively) compels the thought of a special susceptibility of the neural elements in these cases. Of the thirteen members of the second generation, seven died in infancy from obscure causes. Yet the family was not poverty-stricken and its manner of living not unhygienic. Although such an occurrence is not very unusual, yet the fact that the six survivors as well as their children are all affected with one chronic disease or another, naturally impels one to look for a common cause of death and disability in the stricken family.

In the light of the recent discoveries in the field of inheritance, the latter consideration should not appear as altogether far-fetched. Morgan [27] and others have described a Mendelian *lethal* factor in some of the breeds of the *Chrysophila* fly. In the case of the family under description we have seen that the condition of myotonia has been inherited as an independent factor from the first female; and that it has become dominant, that is to say has become manifest as a muscle abnormality, in those cases where the offspring have inherited a large musculature. But there is nothing in the history of this family, as far as it has been ascertained, to prove that the psychosis of the first female was an entirely independent factor from that of myotonia. The fact that in the records of myotonia congenita we find almost universally the muscular disorder associated immediately or mediately with psychopathies, speaks against the independence of the factor of myotonia from that of the abnormal mental state of the first female in this series. And this conjecture is rather corroborated by the fact that a certain number of the myotonics in this family, although free from psychopathy, are not free from neuropathies. After a careful consideration of the facts in connexion with this family, the suspicion has been forced upon the writer that myotonia congenita is caused primarily not by an inherited abnormality of muscular structure or function, but by an inherited sub-lethal factor which exerts an injurious action upon the neuro-muscular system. In seven cases the injurious action of this hypothetical agent was sufficient to determine the balance in favour of death. In other instances the existence of this agent is manifested in myotonia with atrophy of individual muscle fibrils, or of entire muscles and muscle-groups. In still others it causes myotonia, with muscular pains and a diminution of the tendon reflexes, with or without muscular atrophy. In others still, especially in cases where the musculature is not congenitally of large volume, the muscular system is spared, and the action of the inherited injurious agent is upon the highest cerebral structures.

Such a conception of the disease might help to explain not only the singular co-existence of psychoses with the muscular disorder either in different members of the same family or in the same person, but the occurrence of the temporary and acquired forms of the disease as well. If myotonia congenita is caused by an inherited abnormal content of the body fluids, then a temporary myotonia might be caused by a temporary alteration of the contents of the body fluids of a certain kind. Such a temporary alteration of the body-fluids must have occurred in the cases described by Talma [40] with an acute febrile onset and severe gastro-enteric disturbances; and by Schultze [36] in connection with gastric dilatation, associated with the symptoms and signs of tetany. The same principle might be applied to the cases where myotonia has occurred in the course of severe disturbances of the central nervous system, such as the case of brain tumour described by Bremer and Carson [5]; of myotonia associated with athetosis described by Kaiser [22], and of myotonia occurring in connection with syringomyelia, mentioned by v. Frankl-Hochwart [12] and by Schlessinger [35].

A PSYCHOLOGICAL CONCOMITANT OF THOMSEN'S DISEASE.

It will appear from the history taken in connection with Case 2 that the myotonic mother of four myotonic children, and herself the daughter of a myotonic mother, was reluctant to admit that she suffered from any muscular disorder. As a matter of fact she strenuously denied the existence of the disorder in any member of her family, and this denial was maintained for weeks in the face of numerous facts to the contrary.

Such an attitude of mind appears to be a pretty constant concomitant of the muscular disorder, and is mentioned by a number of writers. Jendrassik [19], in his able summary of the affection, mentions the fact that "the patients seek to conceal their infirmity by all-sorts of artifices." Thomsen himself must have been thoroughly aware of this attitude in his own case when he said: "There is an active psychic factor involved, namely, the fear of ridicule. As soon as the feeling arrives that those about will discern and observe the disability, the symptoms become aggravated in the highest degree." In the present case of the mother of the myotonic children there was, in addition to the desire to conceal a lifelong disability that is so thoroughly disguised by an appearance of perfect health and strength, another inhibitory

factor. It was the wish to suppress the consciousness of a responsibility of having transmitted her infirmity to future generations, innocent as she certainly was of any wrong motive at the time when the responsibility was taken.

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A CONTRIBUTION TO THE ANATOMY OF SPINA BIFIDA.

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INTRODUCTION.

THE purpose of this paper is to emphasize certain features in the minute structure of cases of spina bifida which have a direct bearing on details of operative procedure, and on prognosis as regards nervous function after and apart from operation.

Recent medical literature contains few accurate descriptions of specific cases of rachischisis, and the discussion and diagrams in the average surgical treatise are imperfect in detail and often misleading. Since Virchow, Lebedeff and v. Recklinghausen in the eighties, first called attention to the embryological basis of the defect, very little new work has been done, and it appears that this early work has been largely lost sight of. Surgeons have depended upon operative findings which are necessarily incomplete, and pathologists have left these deformities severely alone. It is true that the study of anomalies in many instances is not a fruitful one. To the study of this particular group of abnormalities, however, much practical value attaches, as a large proportion of the less severe types demand surgical relief. The number of cases here reported is small, and the records in some are necessarily incomplete, but material of this nature is difficult to obtain, and especially so in the milder cases round which surgical interest centres.

Before passing to the discussion of individual cases it seems advisable to recall briefly the normal development of the structures which are defective, and the general morphology of the types of defect encountered.

DEVELOPMENT OF CENTRAL NERVOUS SYSTEM AND VERTEBRAL COLUMN.

The central nervous system first appears as a thickening of the surface ectoderm along the mid-dorsal line of the embryo, the medullary

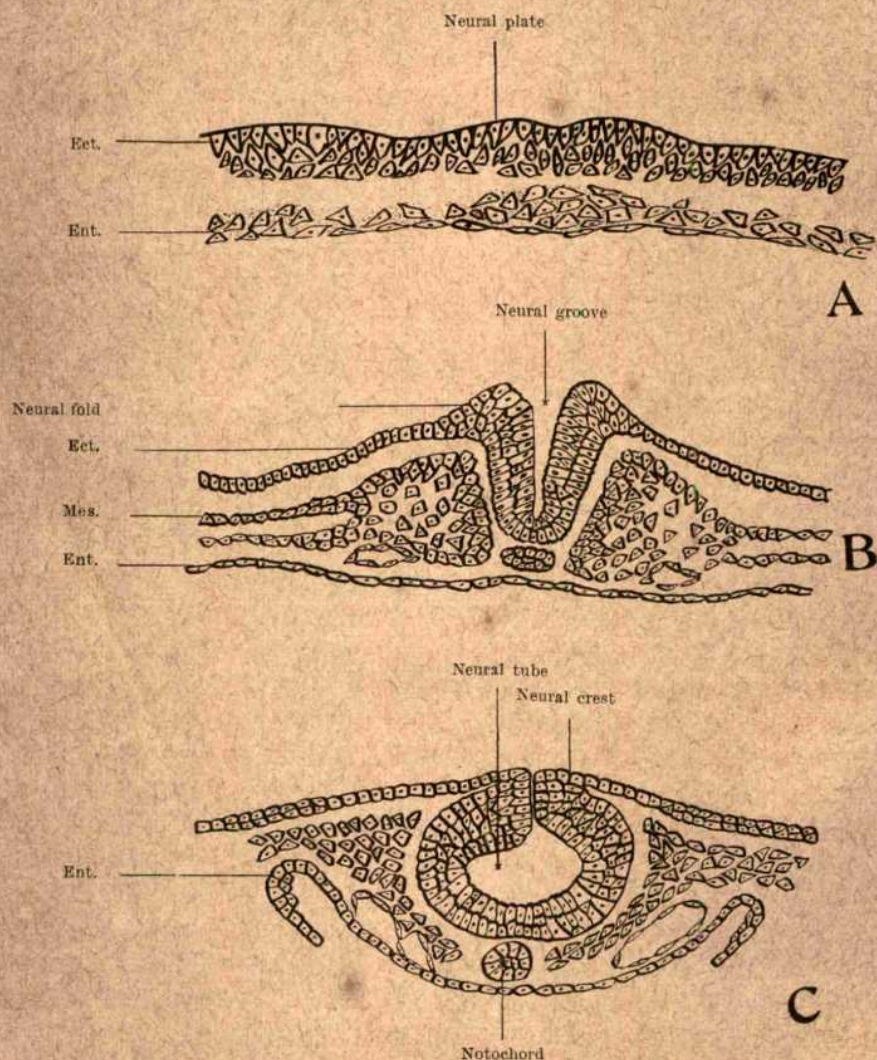


FIG. 1, A, B, C.—Transverse sections of chick embryos, showing stages in the formation of the neural tube.

plate (fig. 1, A). The edges of this plate rise, turn toward the mid-line and finally meet and fuse, forming a closed tube (fig. 1, B, C). Fusion is segmental in character; it takes place first in the cervical region, and

progresses backward and forward, being delayed longest in the cephalic and caudal segments (fig. 3). Ultimately the closed neural tube sinks beneath the surface, mesodermal structures interpose themselves and the neural ectoderm continues its growth independently of the integument. In the regions last closed there remain for some time minute openings, the neuropore at the anterior extremity and the caudopore at the posterior, through which the central canal communicates with the exterior. Ultimately these openings also become closed.

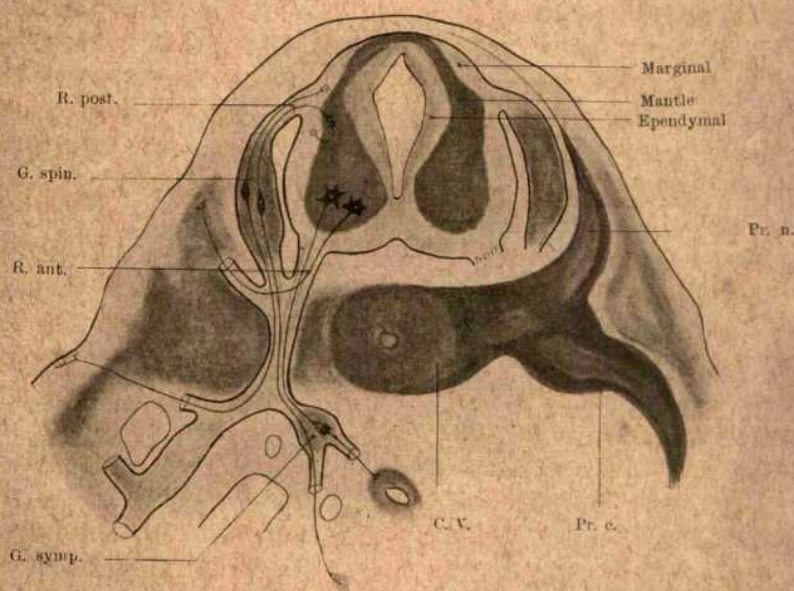


FIG. 2.—Schematic. Left side modified from *Prentiss and Aray*, showing the origin of the spinal ganglia and the spinal nerve roots. Right side represented as though sectioned through vertebral body, showing the early stage of vertebral development with the origin of the neural arch.

In the meantime, even before the medullary folds have completely fused, an increase in size of the cephalic portion of the folds becomes apparent and one can differentiate the brain from the spinal cord (fig. 3). It is not necessary here to deal with the complex further development of the cerebral vesicles, but attention must be confined to that of the cord. In its separation from the surface ectoderm there persists for a time at the mid-line a chain of cells, the neural crest (fig. 1, C), having the characteristics of the cells of the neural tube proper. From this chain are formed the posterior root ganglia (fig. 2, *G. spin.*) and the

ganglia of the sympathetic system (fig. 2, *G. symp.*), as well as the nerve cells found in various viscera.

The further development of the spinal portion of the neural tube consists in the rapid proliferation and specialization of its cells resulting in a differentiation into three zones, outer, middle and inner, distinguished by the grouping and ultimate fate of their cell contents. Certain of the cells become neuroblasts, the forerunners of neurons; certain others, also ectodermal, become supporting glial cells. The inner zone (fig. 2, *Ependymal*) undergoes but little increase; it consists of glial cells only, which form the ependymal lining of the small persistent central canal and the narrow surrounding layer of gelatinous tissue. The middle zone (fig. 2, *Mantle*), containing the neuroblasts, becomes the grey matter of the cord; the outer zone (fig. 2, *Marginal*) becomes the white matter, consisting of the processes from the neuroblasts of the middle zone and of the spinal ganglia, supported in a meshwork of neuroglia.

The middle zone rather early becomes differentiated into an alar, posterior lamina, and a basal, anterior lamina. In the alar lamina are developed the structures of the posterior horn. In the basal lamina are developed the motor nerve-cells of the anterior horn, and the emerging fibres of these pass out as the anterior nerve roots (fig. 2, *R. ant.*) between the segments of the developing vertebræ. Meantime the spinal ganglia which have formed from the neural crest pass ventrally and laterally until they lie in the spaces between the vertebræ, in close contact with the anterior nerve root fibres. From the cells of the ganglia processes pass into the outer zone of the cord and form the posterior roots (fig. 2, *R. post.*) of the spinal nerves. Fibres from these ascend in the posterior columns; others form synapses about the cells of the posterior horn. These relations are shown diagrammatically in the left side of fig. 2, representing a cross section of a 10-mm. human embryo.

While these changes are occurring within the neural tube, mesodermal structures come into relation with it, and form a delicate sheath, which later becomes separated into three layers, pia, arachnoid, and dura mater. Anteriorly, the vertebral column is developing with the notochord, which is shown in fig. 1, A and B, as its point of departure.

The right half of fig. 2 shows diagrammatically an early stage in vertebral development. Surrounding the notochord is the rudiment of the body of the vertebra (*C. V.*), with the beginning of a costal process (*Pr. c.*) and a second process (*Pr. n.*) directed dorsalward and partly enclosing the spinal medulla. This is the neural process from which

develop the laminae and the spinous processes. The laminar processes grow out from the neural process toward the mid-line of the embryo, surrounding the spinal cord and forming the spinal canal. In a foetus

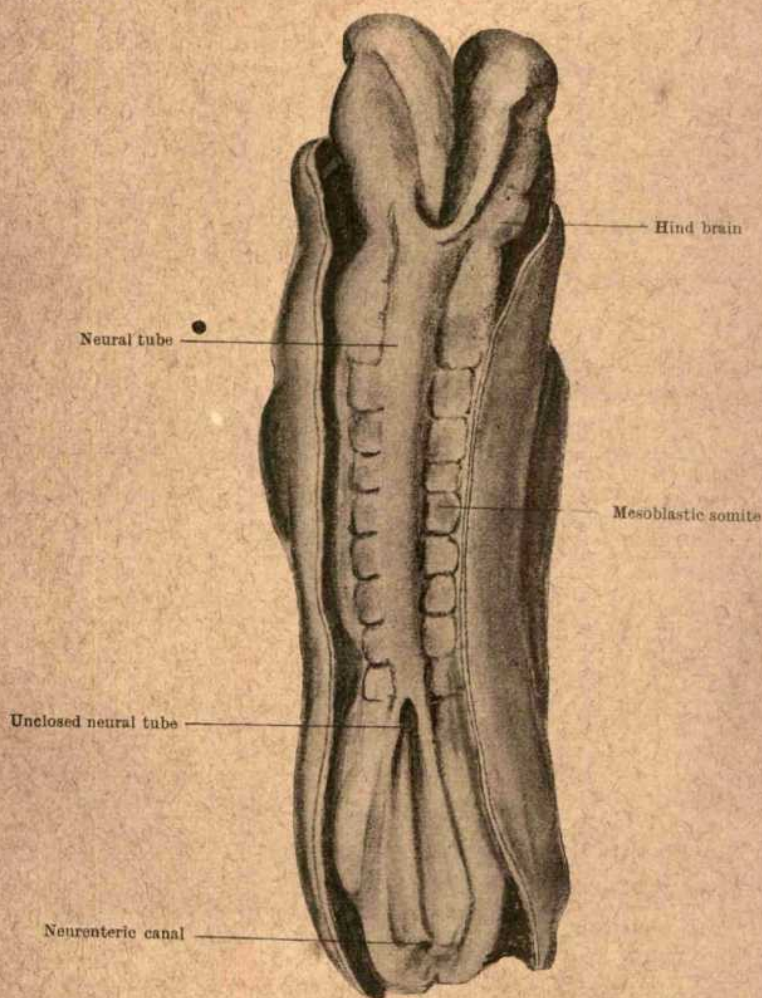


FIG. 3.—Human embryo of 2.11 mm., showing closure of neural tube, and early stage in differentiation of cerebral region. (After Keibell and Mall.)

of 33 mm., about nine weeks, they extend well out towards the mid-dorsal line, and are united across this by a membrane of connective tissue. In one of 50 mm., about the eleventh week, they are united so as to form a canal similar to the adult spinal canal, and small spinous

processes are developed upon them. The completion of the spinal canal takes place earlier in the thoracic than in the cervical and lumbar regions.

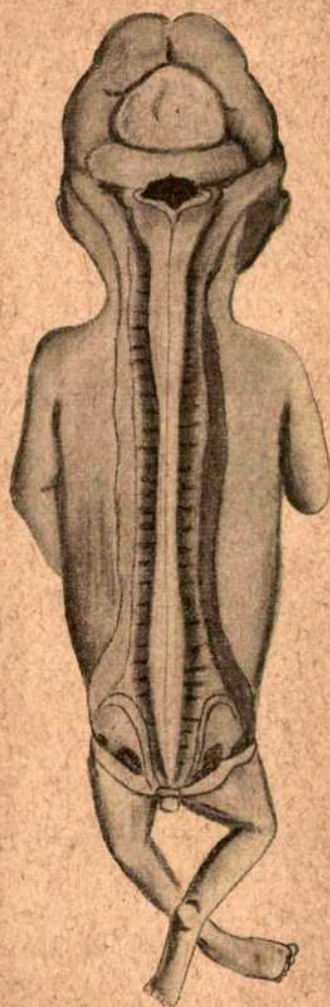


FIG. 4.—Human embryo, aged 3 months, showing the spinal cord extending to tip of coccyx. (After Keibel and Mall.)

During this period, as is shown in fig. 4, the cord extends throughout the whole length of the spinal canal, and the nerve roots and spinal ganglia formed in each segment take up a position between the bases of the neural arches, in the future position of the intervertebral for-

mina. Growth of the neural tube and of the vertebræ progresses at equal rate until the third month, and up to this time the nerve roots continue to pass out of the canal perpendicularly to the long axis of the cord. Fig. 5, A, shows a diagrammatic representation of the relative positions of neural and of vertebral segments at this stage. In the further growth of the embryo, however, the growth of the neural tube is outstripped by that of the vertebral column, and as it is anchored above by its attachment to the medulla it remains high in the canal, terminating at birth at the level of the third lumbar vertebra (fig. 5, B). This is usually referred to as "the upward migration of the cord." At the tip of the coccyx, the extremity of the cord remains for a long time connected with the surface (fig. 5, A), and this connection pulls the end of the cord and the pial sheath into the slender filum terminale (fig. 5, B). It will be necessary to describe this in greater detail later, as it has direct bearing on the defects which occur at this region of the neural canal. The spinal nerves, having a fixed relation to the intervertebral foramina, are carried away from the cord segments with which they are connected by the growth of the vertebræ. Their roots elongate to compensate for the unequal growth, so that while those from the upper segments continue to pass out almost horizontally, those from the lower segments descend more and more within the canal as one passes downwards. At birth a cauda equina is found similar to that in the adult. Fig. 5, B, shows schematically the relation of cord, spinal ganglia and nerve roots as they are found in the full-term foetus; it does not differ materially from that in the adult. It should be mentioned that in making fig. 5 the skeletal basis of the diagram was drawn to scale from an actual dissection in a seven months' foetus. For purposes of comparison this skeletal scheme was used for all the diagrams in this figure, as the particular change under consideration seemed better brought out in this way.

The formation of the filum terminale and its relation to the coccygeal segments of the cord has a direct bearing on the structure of lumbosacral spina bifida as it differs from spina bifida in other areas of the neural tube, and must therefore be discussed in slightly greater detail. The coccygeal segments, with the exception of the first, are rudimentary. Their cells do not differentiate beyond the embryonic stage of a layer of glia cells surrounding a central canal. The last coccygeal segment remains attached to the surface ectoderm, and with the increased growth of the vertebræ this undifferentiated area becomes drawn out into a slender thread of glia in which for a long time there

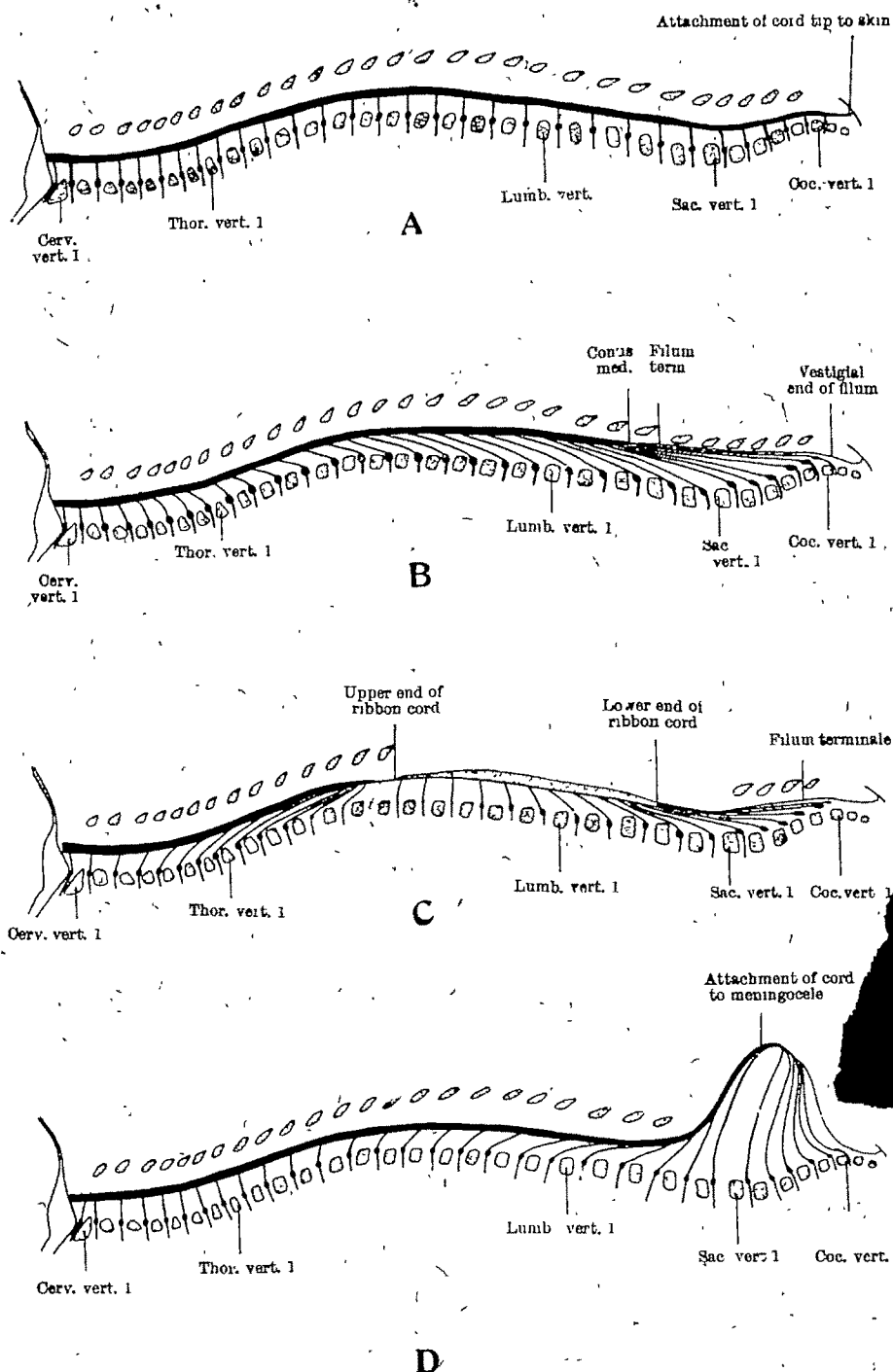


FIG. 5, A, B, C, D.—Diagrammatic representation of migration of cord and relations of nerve roots: A, in 8 months' fetus; B, in fetus at term; C, in Case I, myelocoele; D, in Case III, myelomeningocele. The skeletal basis of all the figures was taken from a dissection of the spinal column of a 10 months' fetus.

is a persistent central canal. It remains attached to skin by its tip, and higher up in the rudimentary coccygeal part of the spinal canal it is separated from the skin only by imperfectly differentiated meningeal layers, and by a band of fibrous tissue which alone represents the vestigial coccygeal laminæ (fig. 5, B). Even in the full-term foetus nervous elements can still be found in it. The filum terminale as low down as it remains glial represents, therefore, the lower four coccygeal (tail) segments, which have become drawn out so that they stretch from the tip of the coccyx to the level of the first coccygeal cord segment which lies at the level of the third lumbar vertebra. The normal adherence of the end of the cord to the skin surface, and its persistent rudimentary state in this region, have a direct effect in producing one variety of meningocele found in this region of the spine.

MORPHOLOGICAL BASIS OF SPINA BIFIDA.

It is not within the scope of this paper to enter into the underlying causes, probably of a bio-chemical nature, which determine the occurrence of spina bifida and of other basic developmental defects. It is necessary merely to point out the morphological factors which are concerned in this particular class of cases.

Apparently the mechanism of closure of the medullary folds is one of the most delicately adjusted of developmental processes, for anomalies are of fairly frequent occurrence both in man and in other vertebrates. In chick embryos which have been improperly incubated it is a common experience of the embryologist to find a number in which the folds have partly or entirely failed to unite in the usual time sequence with other organs. Usually very young embryos only present this deformity, probably because the older individuals die from the unfavourable conditions which have produced the defect. Other laboratory embryos, as opossums, pigs, &c., present the defect more rarely, doubtless because of the normal conditions of their existence, as these embryos are fixed and prepared in utero, and not artificially incubated.

It will be seen that any interference with the closure of the medullary folds will, of itself, cause a corresponding interference with the development of the neural arch of the vertebra forming around that region of the cord. Any defect, however slight, involving the medullary tube proper, is associated with defect of the vertebral neural canal. Such medullary tube defect has morphologically a wide range of possibilities, from mere delay in the closure of the caudopore with a consequent delay in the development of the membranes of the cord in this region and of the integument covering them, to a complete lack of the infolding

of the medullary plates, with or without differentiation of the neural ectoderm forming the plates. In certain cases the defect in the medullary tube has been so slight or so evanescent that in the fully developed embryo no trace of defect remains in the cord itself, but its existence is revealed by an imperfection of membranes associated with a corresponding defect in the vertebral canal. In still other cases, one finds no such definite evidence of an original medullary tube defect, the anomaly consisting merely of a failure in the fusion of the vertebral spines or of the laminae. More rarely laminae are partly or wholly absent. This is probably also dependent in a proportion of cases on medullary tube defect, for nervous symptoms are not infrequent. Reference will be made to this later in the discussion of the types of spina bifida encountered in actual specimens.

It will be seen that all these variations of the deformity may occur throughout the entire length of the medullary tube, or may be limited in extent. The development of the cephalic extremity of the tube and of the cranium is so divergent from that of the spinal cord that no attempt will be made in this paper to discuss defects involving the brain (cranio-rachischisis). It must be remembered, however, that defective development of one part of the neural tube is prone to be associated with defective formation of other parts, and cephalic abnormalities are frequently found with spinal. Fusion of the spinal part of the medullary folds tends to be normally later in the cephalic and in the caudal ends of the embryo than in the mid-thoracic regions, and local defects are more apt to occur at these points; but the fusion is segmental in character and segments at any region may fail to unite without necessarily impeding the union of segments above or below. The rudimentary character and morphological peculiarities of the coccygeal segments (filum terminale) already alluded to may be responsible for the great number of defects occurring in this region.

It is particularly necessary to remember the time sequence of the structures which participate in the defect. Normally the entire neural tube is closed at the end of the third week, it is then the full length of the embryo. Normally the vertebral neural arches from the first cervical to the third or fourth sacral are closed at 50 mm. (eleventh week); the arches below the fourth sacral are normally rudimentary. The defect, whether it be a failure of closure of the medullary groove, or an adherence of meningeal layers to skin, cannot occur after the vertebral arches are closed; and at this period of growth and indeed for a short time thereafter (third month), the vertebral column and

by imperfect epidermis and adherent to the presenting meninges. To this imperfect skin the term "parchment" is fittingly applied; it is poorly vascularized and of low vitality. On opening into the sac and examining its walls one may find a variety of conditions. (1) The sac wall may be composed of fused dura and arachnoid, or of these two layers in close proximity but not fused, forming a distended single sac representing the subarachnoid space, in the bottom of which the cord courses down covered by pia in the normal manner. (2) The dura and the arachnoid may be separated by a collection of fluid, the tumour consisting of an outer dural and an inner arachnoid sac, the pia and cord being normal. (3) The outer layer of pia may be likewise distended, forming a third, usually much smaller sac, within which the cord lies. (4) In any one of these forms the cord may be lifted up by the fluid round it, and may course through the middle of the cyst, presenting, however, no obvious abnormality. This condition, however, does not seem to be well authenticated.

Class 2.—Mesoblastic defect with slight epiblastic defect: (rachischisis incompleta restricta).

(A) *Myelo-meningocele.*

Here we find a meningocele in which the neural tube has closed but has remained in contact with the surface ectoderm in a small part of its extent, the result of delayed closure usually near the caudopore. The cord is drawn by adhesions to the surface of the sac, and is attached by a greater or less portion of its length to the sac wall. The nerve roots may pass down from its ventral surface to reach their foramina, or may be caught in the adhesions and course down over the surface of the sac. These cases are always covered by parchment skin, but by the microscope integumentary structures may be demonstrated lying dorsal to the neural tube. This variety is probably confined to lumbosacral rachischisis, and is the result of the peculiarity of the development of the coccygeal segments already noted; it is, however, often confused with more severe types in which some cord segments have not closed, and many cases described in this class more properly belong to Class 3 (A).

(B) *Hydro-myelo-meningocele.*

In certain cases in which the neural tube has closed, either with or without a persistent adherence to the surface ectoderm, as was described above, the central canal of the cord becomes enormously distended by fluid, and within a meningeal sac of any of these types

a medullary sac may be found, the wall of which is formed of thinned nervous tissue, from which more or less perfect nerve roots pass. This form is not infrequently encountered, and is entitled to separate mention because of the importance of differentiating it from the pure meningocele which it resembles clinically. It represents only an exaggerated form of the concomitant hydro- and syringo-myelia which are so frequent in the more severe grades of rachischisis.

Class 3.—Gross epiblastic defect with accompanying mesoblastic defect (rachischisis completa).

(A) Myelocoele (Rachischisis Completa Restricta).

Here two or three segments of the medullary folds have remained open and the neural ectoderm lies exposed on the surface of the body as a ribbon of delicate tissue down the mid-dorsal line. On either side the meninges are attached to the edges of the medullary ribbon, and form a zone of parchment skin which passes in turn into normal skin. In certain cases no collection of fluid occurs, but in the majority the meningeal layers become filled with fluid as in pure meningoceles, and the open neural ribbon is stretched over the surface of a tense sac. Cases of this type occur in the cervical region, very rarely in the thoracic, but often in the lumbo-sacral region. In the cervical and thoracic regions they are easily differentiated, but in the lumbo-sacral they are apt to be obscured by the growth of surface ectoderm over the lower part of the neural ribbon. The lower coccygeal segments, functionless in man, never develop beyond the simple neural tube of the embryonic state. The last coccygeal segment normally remains attached to the skin. The tendency of all these segments is towards atrophy rather than growth, while the growth of skin ectoderm is as active as elsewhere in the body. If the upper coccygeal segments do not close, the few neural cells present in them tend to become atrophic and overgrown by skin, and this part of the neural tube is prevented from elongating into the filum terminale. The adhesions to skin so formed mechanically drag down the sacral segments and involve them in the defect. In the lumbo-sacral variety also, probably as a result of the adhesions to skin, fluid is especially apt to collect in large quantity, and its pressure within the meningeal sac may be so great as to draw the normal cord above the open segments down out of its canal and into the sac. Thus a normal cord may appear to end in the middle of the sac wall, and the open medullary groove segments below may be covered by inflammatory exudate or by overgrown integument so that

the significance of cord attachment is entirely overlooked. Careful study will probably result in placing many of the cases which have formerly been placed in Class 2 (A)—rachischisis incompleta—in this class with other complete defects.

With these, as in other cases of cord involvement, hydromyelia and syringomyelia are often associated.

It is customary to refer to the cases of this type in which the meninges are filled with fluid as cystic myeloceles, but while this term has some descriptive value it does not denote any class distinction.

(B) *Myelocele (Rachischisis Completa Partialis or Totalis)*.

These cases do not differ from those in Class 3 (A), except in the extent of the defect, which involves a very large number or all of the neural segments. Because of the extent of the defect there is never an accumulation of fluid in the severer cases. The neural tube lies flattened out in the groove formed by the undeveloped vertebral laminae upon the surface of the exposed vertebral bodies. The meningeal layers are developed beneath it and pass laterally into a zone of parchment skin which blends with the normal skin. In the cases of total defect, where there has been no abnormal adherence of the cord to the skin over the coccyx, the ribbon cord may migrate upward as in the normally developed cord, and here the lower sacral vertebrae may continue their development, without interference by the neural defect. Total neural lesion may therefore occur without total vertebral defect. This is important because of its bearing on the problems presented by the restricted lesions of the same class.

In both the types just mentioned the medullary tissue may present wide variations in the extent to which the differentiation of its cells has occurred. In some instances the condition remains embryonic, and no trace of the adult medullary structures is to be found; in others the cord substance has developed as though closure of the folds had been accomplished, and the nerve cells and roots can be easily distinguished.

Statistics of the percentage occurrence of spina bifida in its various manifestations are difficult to collect. From observation in the anatomical laboratory it appears that mere vertebral defect is of fairly frequent occurrence. Various forms of meningocele come frequently to the attention of the surgeon, but are infrequently reported, so that no accurate idea of their frequency can be formed. The cases with marked medullary involvement are often born dead, or succumb shortly

to infection. As they are not remediable, they attract but little interest on the part of the obstetrician.

Surgical interest centres about the cases of spina bifida restricta, since it is in these cases that operative interference is feasible. Here, however, while more case records are available, their imperfect nature and the varied use of descriptive nomenclature makes accurate classification a matter of extreme difficulty. This is especially true of those of Class 2, in which there is involvement of the cord.

Before going further it will be advisable to discuss the few cases here studied in detail, and to point out the difficulties of recognizing the types from operation or gross dissections only.

DISCUSSION OF CASES.

Method of preparation and study of specimen.—The material studied is partly operative and partly pathological museum specimens. The conditions under which it was obtained made certain features of the accurate study difficult. In the three operative cases (Cases III, IV, VII) it was the writer's good fortune to assist at the operation and in the care of the patients, so that the observations on these were carried out as a continuous first-hand study. In each case drawings were made from the actual specimens, enlarged to scale, and wherever any matter of personal interpretation of the condition modifies the diagrams it is clearly indicated in the description. It will be obvious that certain features of a preserved specimen can be brought out only by personal observation.

In making the microscopic study of the specimens, blocks of tissue of 2 to 3 mm. thickness were cut, embedded in celloidin, and stained by the following methods: (1) toluidin blue; (2) iron hæmatoxylin; (3) hæmatoxylin-eosin. In one or two cases other methods were tried, but as they were not fruitful they were abandoned. All the sections from each block were stained and examined, and the interpretation of certain features in the individual sections was frequently the result of this study. In certain cases where the condition was obscure additional sections were made above and below the original blocks, but detailed description of these is not given. The sections photographed and described are those which appear to throw most light on the anatomical and clinical aspects of the cases. All the photographs were made with a $\frac{1}{4}$ in. objective and reduced to the same scale, so that comparison of their size could be made. They were re-touched with indian ink with constant reference to the slide from which they were made, in order to indicate myelination and nerve cells.

CASE I.

Myelocèle—spina bifida completa partialis, of Class 3 (B). Specimen No. 1109, Surgical Pathology Museum.

The specimen was received as part of a pathological collection which came into the department of Surgical Pathology of the University of Texas, and no history could be obtained. The preservation was not all that could be desired, and no care had been taken to protect the myelocèle from injury in transportation. The body was in good condition, however, except for the more delicate neurological examinations of the brain. The body was that of a negro female foetus, length 24 cm. from vertex to coccyx. External appearance is shown in fig. 6. Limbs and trunk were well developed in form and musculature. External genitalia and anus normal. Head is hydrocephalic, circumference 41 cm. (occipito-frontal). Face and oral cavity normal. Spina bifida completa extends from level of eighth thoracic vertebra to that of the upper margin of sacrum.

Dissection.—On opening the ventral body wall a diaphragmatic hernia is seen, the greater part of the abdominal contents occupying the left thoracic cavity. The right side of diaphragm is normally developed, the left side presents a widely open pleuro-peritoneal hiatus, through which the whole of the stomach, small intestine, appendix, the first part of colon, spleen, and left lobe of liver protrude into left chest. The heart and pericardium are normal except that they are pushed to the right of the mid-line by the herniated viscera. Right lung is normal in shape, atelectatic, smaller than normal on account of pressure: left lung is very small, about one-fourth normal size and flattened. Thymus is displaced toward the right, but otherwise normal. Examination of the abdomen shows it to be occupied by the right lobe of liver, which is normal except for a distortion in shape due to the herniation of its left lobe and to the abnormal position of the other viscera, and by the descending colon and a large convoluted sigmoid, which occupy their normal positions. The adrenals and the genito-urinary system are normal.

Microscopic examination of the organs was not made, as they gave no sign of structural abnormality.

Skeleton.—Maceration for slight anomalies was not done because of the desire to keep the specimen for demonstration purposes. So far as could be ascertained without maceration, the skeletal system is normal excepting that the head is typically hydrocephalic, its sutures very wide, and the bones very soft. The base of skull and the cervical and upper seven dorsal vertebrae are normal. The lower five dorsal and all the lumbar vertebrae have large flaring laminae which are curved with the convexity anterior, so as to present on the dorsal surface a wide shallow ditch. The prominences of these laminae are clearly distinguishable beneath the thin parchment skin of the region (fig. 7). Ossification centres are normal in site and size, in the bodies and laminae. The sacrum is normal.

Nervous system.—Accurate examination of the brain was impossible because

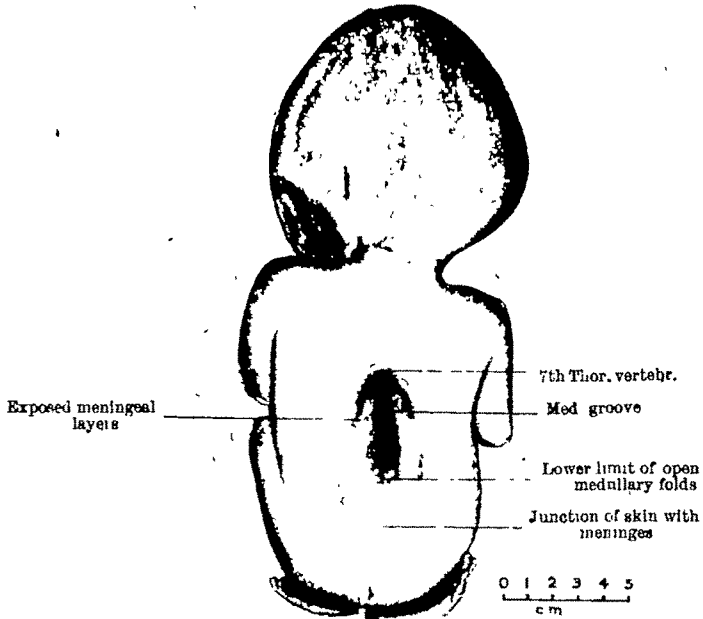


FIG. 6.—Case I, myelocoele. External appearance of specimen before dissection.

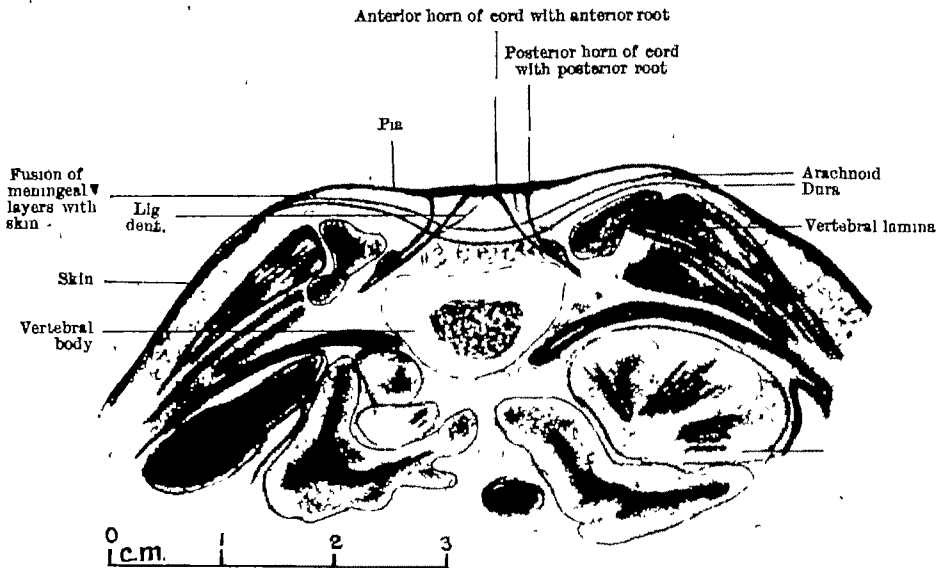


FIG. 7.—Case I, myelocoele. Cross section through region of twelfth thoracic segments of the cord.

CASE I.

Myelocele—spina bifida completa partialis, of Class 3 (B). Specimen No. 1109; Surgical Pathology Museum.

The specimen was received as part of a pathological collection which came into the department of Surgical Pathology of the University of Texas, and no history could be obtained. The preservation was not all that could be desired, and no care had been taken to protect the myelocele from injury in transportation. The body was in good condition, however, except for the more delicate neurological examinations of the brain. The body was that of a negro female foetus, length 24 cm. from vertex to coccyx. External appearance is shown in fig. 6. Limbs and trunk were well developed in form and musculature. External genitalia and anus normal. Head is hydrocephalic, circumference 41 cm. (occipito-frontal). Face and oral cavity normal. Spina bifida completa extends from level of eighth thoracic vertebra to that of the upper margin of sacrum.

Dissection.—On opening the ventral body wall a diaphragmatic hernia is seen, the greater part of the abdominal contents occupying the left thoracic cavity. The right side of diaphragm is normally developed; the left side presents a widely open pleuro-peritoneal hiatus, through which the whole of the stomach, small intestine, appendix, the first part of colon, spleen, and left lobe of liver protrude into left chest. The heart and pericardium are normal except that they are pushed to the right of the mid-line by the herniated viscera. Right lung is normal in shape, atelectatic, smaller than normal on account of pressure: left lung is very small, about one-fourth normal size and flattened. Thymus is displaced toward the right, but otherwise normal. Examination of the abdomen shows it to be occupied by the right lobe of liver, which is normal except for a distortion in shape due to the herniation of its left lobe and to the abnormal position of the other viscera, and by the descending colon and a large convoluted sigmoid, which occupy their normal positions. The adrenals and the genito-urinary system are normal.

Microscopic examination of the organs was not made, as they gave no sign of structural abnormality.

Skeleton.—Maceration for slight anomalies was not done because of the necessity to keep the specimen for demonstration purposes. So far as could be ascertained without dissection, the skeletal system is normal excepting that the skull is hydrocephalic, its sutures very wide, and the bones of the face are soft. The cervical and upper seven dorsal vertebrae are normal, the lower five dorsal and all the lumbar vertebrae are malformed with the convexity anterior, so

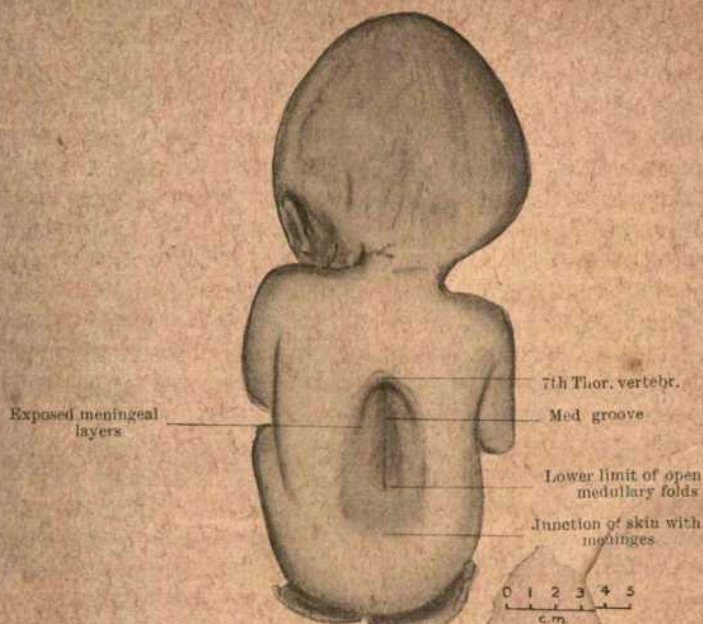
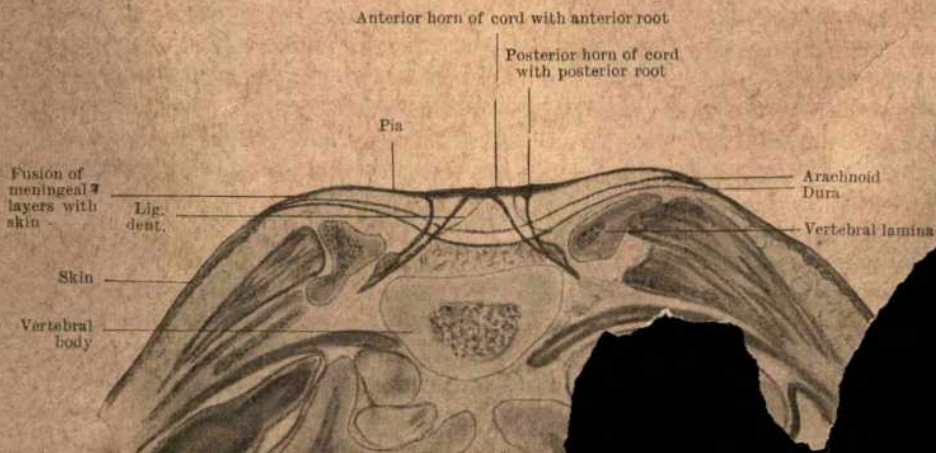


FIG. 6.—Case I, myelocoele. External appearance of specimen before dissection.



of the imperfect preservation of this portion of the central nervous system. The lateral ventricles are greatly distended with fluid and the cerebral cortex is thinned to a layer varying from 4 or 5 mm. to the thinness of tissue paper. The choroid plexuses of the lateral ventricles are large, but present no other apparent abnormality. The cerebellum is poorly preserved and appears to

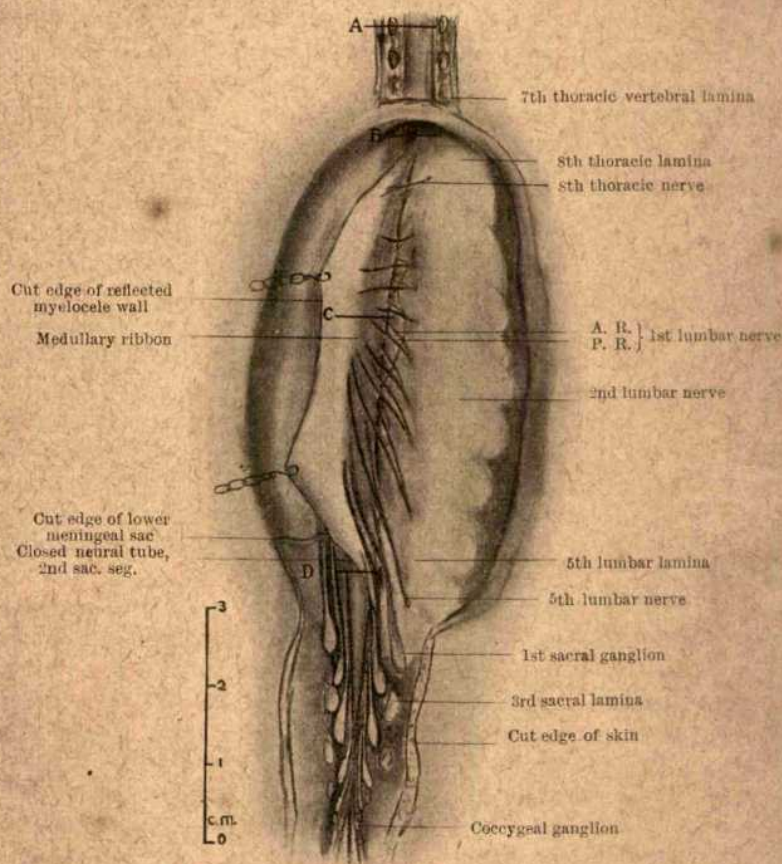


FIG. 8.—Case I. Dissection of myelocoele, by reflection of lateral wall and opening the spinal canal above and below the lesion. Levels of the microscopical sections indicated by letters A, B, C, D.

be represented by a mass of loose hæmorrhagic and very vascular connective tissue, with a small amount of nervous tissue at its base, apparently representing the peduncles. The mesencephalon, pons and medulla are macroscopically normal.

The spinal canal was opened from the foramen magnum to the level of the

seventh thoracic vertebra, i.e., the last normal vertebra. The meninges in this region are normal. On exposing the cord it is found to be superficially normal from the medulla oblongata to the level of the sixth thoracic vertebra; but the portion lying on the body of the seventh thoracic vertebra is small, soft and membranous, and terminates by passing under the seventh neural arch to blend with the myelocoele below.

The arrangement of the nerve-roots from this whole region of cord is peculiar. The first two cervical pairs pass out almost horizontally; those below incline more and more *upward* in the canal, as is shown diagrammatically in fig. 5, C, so that the roots which pass through the first thoracic foramina come from the cord which lies in relation to the fifth thoracic vertebra. All the roots to this level are large and apparently normal except for their upward direction. At the level of the sixth thoracic vertebra the roots are very delicate, and it is not possible to trace them all, but attenuated fibres from this region appear to enter the second, third, fourth, and fifth foramina (fig. 5, C). From the membranous portion of cord lying on the seventh thoracic vertebra delicate strands pass to the sixth foramina, and possibly also to the seventh, though these may arise from the open cord below.

It is necessary here again to direct attention to figs. 5, A and B, illustrating the normal upward migration of the cord in the spinal canal. In this specimen the seventh thoracic segment of the cord was prevented from moving upward by adherence to the myelocoele below. This portion of cord, therefore, represents the segment of neural tube infolded in this body segment of the embryo, and its roots pass out horizontally as they were originally laid down. They are attenuated because the normal development was hindered by the adhesions and by traction, as the length of the spinal canal above them increased. Similarly the upper cervical segments maintained their normal relationships by virtue of their attachment to the brain stem, and their roots pass out horizontally as is usual. If all the medullary tube had developed equally between these two fixed points, the preponderant growth of the vertebral canal should have resulted in an equal stretching of the whole length of the cord, the nerve-roots continuing to pass out horizontally. We find however, that the lower portion of cord is membranous, and its small nerve roots show that it has fallen far short of attaining its normal growth; moreover, being largely composed of connective tissue (membrane), it has apparently been much less easily stretched than the higher portions, and has remained almost stationary while the better developed higher segments have been pulled down to its level. A greater descent of the lower cervical segments would be expected, but the inequality of growth of the cervical vertebrae and cervical cord in this specimen is less than the inequality in the thoracic region.

As will be seen later in the description of the myelocoele, the nerve-roots below the level of the eighth segment of the cord are also affected by the fixed relations of this cord segment to its vertebral segment, but as the caudal extremity of the cord is not fixed, the cord migration is all upward, and the nerve-roots are carried downward to their foramina, though not to such a great extent as in a normal canal. (See fig. 5, C.)

Myelocoele.—In reading the description of the myelocoele, it is necessary that constant reference be made to the accompanying diagrams. These were made from the actual specimen and dissections: fig. 6 was drawn life-size and reduced, fig. 7 and fig. 8 enlarged to scale and reduced.

Dissection of the myelocoele.—The arch of the seventh thoracic vertebra and the tissues and skin covering it are, as already mentioned, normal in character. At the lower border of this arch, however, as shown in fig. 6, the skin dips down over it and becomes merged in the parchment skin of the myelocoele. From the level of the eighth thoracic to the upper margin of the first sacral vertebra lies a translucent membrane of parchment skin, which merges below and laterally at a distance of 10 mm. from the mid-line, into normal skin. Down the middle of this (fig. 6, *Med. groove*) lies a ribbon of soft friable tissue, which passes above into the neural canal of the seventh thoracic vertebra where it is continued into the spinal cord. Below, at the level of the fourth lumbar vertebra, it sinks under the glistening parchment, and passes beneath to enter the spinal canal in the sacrum. This velvety ribbon represents the open medullary tube, and its structure will be examined more carefully later.

On cutting through the parchment near its junction with skin laterally, it is found to be composed of an inseparable fusion of the three meningeal layers of the myelocoele with the integument. The epithelium of the integument is here very thin, but presents its normal stratification. Passing toward the mid-line a point is reached where the parchment can be separated into its component layers, and at this point all trace of epithelial covering is lost. The relations of the meningeal layers can best be seen in a cross-section through the middle of the myelocoele shown in fig. 7. The most superficial of these layers, viz., the pia, is found to be attached to the medullary ribbon. Anterior to this is a definite arachnoid, and still deeper a thick dura. These are in close contact and are joined by delicate adhesions, which become closer as the lateral edge of the parchment is reached. The line of fusion of the three meningeal layers with skin corresponds closely with the outermost edges of the exposed vertebral laminae. When an incision is made medial to this line of fusion and the pia is reflected, the medullary ribbon is lifted with it, revealing the condition shown in fig. 8. Posterior nerve-roots are seen to emerge from the lateral edge of the ribbon, and anterior roots more medially. Between the radicles the denticulations of the ligamentum denticulatum pass from the pia to the dura; but a few of these, as shown in fig. 7 (*lig. dent.*), pass medially to the anterior roots. The nerve roots pass through the sub-arachnoid space and into the intervertebral foramina, each carrying with it a sheath of dura and arachnoid in the normal manner. Those from the eighth and ninth segments are very delicate, and on these rudimentary posterior root ganglia are found, but in the lower segments the roots and ganglia are more nearly normal in size. The position of the ganglia is normal with reference to the intervertebral foramina. The roots from the upper four involved segments (thoracic 7, 8, 9 and 10) pass out directly to their foramina, without descent

in the canal, in the manner shown in fig. 8, and diagrammatically in fig. 5, C. The roots from lower segments incline downwards before emerging, and finally those from the lowest segments pass under the closed meningeal sheath of the lower part of the myelocoele already seen in fig. 6, at the level of the fourth lumbar vertebra. On dissection (fig. 8), this meningeal sheath is found to be composed of the three fused meningeal layers, which are adherent for a distance of about one millimetre to each other and to the cord. Almost immediately they become separated into their component parts and lose their adherence to the cord, which is closed from this point down. The cord as it passes under the meningeal covering is flattened, but otherwise normal in appearance, and the nerves surrounding it form a typical cauda equina. As will be expected from a study of the diagram in fig. 5, C, the conus is lower in the canal than normal, and the cord terminates at the level of the third sacral vertebra. Except for this the cord and membranes, which at the level of first sacral vertebra become covered by skin, are quite natural after they enter the sacral canal.

Microscopical examination.—Sections were made of cerebellum, pons and medulla, and at various levels of the cord. The fixation of the brain was not sufficiently good to warrant detailed study. The cerebellum has a fairly well-formed corpus dentatum, and the folia, which are few in number, present a definite cortical layer. The pons contains transverse fibres and lemniscus, both myelinated. Cells of the nuclei pontis are not differentiated. In the oblongata the inferior olivary nucleus is well developed, and the medial lemniscus, the emerging fibres of the sixth and seventh nerves, and entering fibres of the vestibular nerve are myelinated and occupy their normal positions. In all the sections there is a looseness of the tissue and a paucity of fibres and cells even where the general structure is most nearly normal; many small areas occur in which the neuroglial meshes are filled with fluid, and in other parts there is an appearance of oedema of the cells. There are many cells which do not appear to be differentiated into supporting and nerve elements; some perhaps represent neuroblasts.

In studying the sections of the cord it will be necessary to refer to the undissected specimen (fig. 6), and to fig. 8 in which the levels of the sections are indicated, and to recall that a "segment" of the cord is numerically determined by the relationships of its nerve roots, and not by its position in the spinal canal. In this case, as had already been seen, the nerve roots behave in a most irregular manner, and it is only by tracing the connections of the section of cord studied that its segmental position can be determined.

Section A (fig. 9, A).—Level of fifth thoracic vertebral segment (first thoracic segment of cord), above lesion. Sections show a normal central canal lined by an ependymal layer. Cells of the anterior horn of grey matter are well formed and their distribution corresponds with that of normal cord of first thoracic segment.

Cells of the posterior horn, difficult to distinguish even in normal cords, cannot be definitely differentiated. It is probable that a small group of them

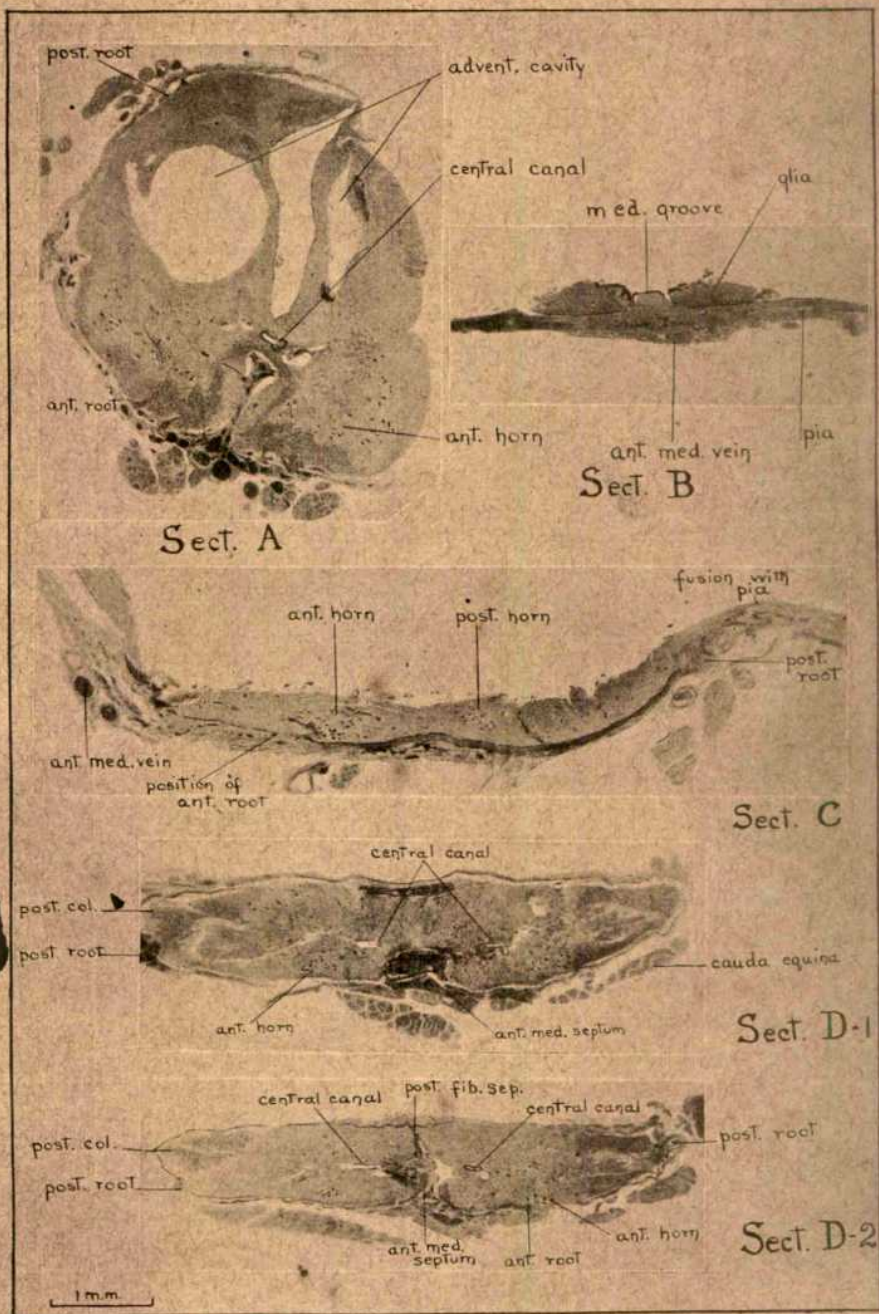


FIG. 9.—Case I, myelocoele. Photomicrographs of sections at the levels indicated in fig. 8.

can be made out in the region indicated in the photograph. The posterior portions of the cord on each side are partially replaced by spaces which occupy roughly the position of the posterior columns, the ascending fibres of which have been interrupted in their course by the imperfect development of the cord below. These and similar spaces in other sections to be described are not artefacts, as is evident from the good preservation of the surrounding structures. The ventral cerebro-spinal tract is normal in size and position, and non-myelinated. This tract normally becomes myelinated late in intra-uterine life. No other long tracts can be distinguished. The antero-lateral fasciculi proprii of each side are myelinated; and there are some other scattered myelinated fibres which may be also regarded as association fibres. The surrounding area is composed of neuroglia and of non-myelinated nerve fibres. The anterior and posterior nerve roots are myelinated and occupy their normal position.

Section B (fig. 9, B).—Upper limit of myelocoele, level of eighth thoracic vertebra, eighth thoracic segment of cord. At this situation, as shown in the photograph, the cord is represented by a layer of poorly differentiated tissue, two or three cells in thickness (*med. groove*), the open medullary folds. (Compare fig. 1, A). These cells are prolonged for a short distance lateral to the mid-line, but no continuous cell layer can be followed between them and the epithelial surface of the adjoining skin; apparently it has been destroyed in handling the specimen. On either side of this open medullary groove is a small mass of irregular tissue (*glia*) composed of nerve fibres and neuroglia. The tissues beneath are poorly formed pia and arachnoid, and small vessels from these layers penetrate the glial masses; laterally they fuse and pass into the corium. No differentiated nerve cells can be found in any portion of this section. The growth of ascending tracts has apparently been blocked below this region by the adherence of the membrane in the myelocoele, but the lateral glial masses undoubtedly contain a few fibres ascending from the cord below. These are in turn blocked at the upper limit of the myelocoele with resulting absence of the posterior columns noted in Section A. Similarly the descending tracts are blocked at the upper limit of the defect and only those which are formed in the cord below this level are to be found in lower sections.

Section C (fig. 9, C).—Middle of myelocoele, level of twelfth thoracic vertebra (first lumbar segment). At this level the ribbon of medullary tissue shows a remarkable degree of differentiation into its usual foetal characters. Large anterior horn cells lie near the median line, and a small group of posterior horn cells lateral to them. Small anterior and posterior nerve roots emerge and enter in relation to these cell groups. They are non-myelinated. The substantia gelatinosa is well developed. The remainder of the ribbon is composed of an indiscriminate mass of neuroglia and nerve fibres, none of which are myelinated. The nerve fibres noted in Section B evidently ascend from the cells in this region. The ependymal layer is destroyed, but a depression corresponding with the central canal is found at the median line. The posterior surface is composed of glial tissue and unmyelinated fibres traversed

by delicate fibrils of connective tissue coming from the pia and containing capillary vessels. This glial layer extends laterally for a considerable distance, and is probably augmented by fibres from the tracts ascending from below. Anterior to the medullary ribbon the pia lies in contact with the nervous layer; it is thicker than is normal and contains many vessels and some leucocytes. In it lie bundles of nerve fibres, some of which appear never to join the cord but to be lost in the meningeal tissue. Sections from the lower part of the ribbon cord show the same structure, but the nervous tissue is broken up by many minute blood-vessels, and a delicate vascular plexus extends over the whole dorsal surface from one lateral pial margin to the other.

Where the ribbon cord closes and passes under the meningeal layers, serial sections were made in an effort to find the transition stages. The nervous tissue in the upper of these sections is so obscured by penetrating capillaries that little information can be gained from them. In the upper sections the anterior medial septum sends two lateral trabeculae, which pass laterally; at the end of each there is found a slightly elongated ependyma-lined cavity. It has not been possible to trace the ependymal cells to the surface of the cord in any of the sections. At a slightly lower level the fibrous septa disappear, but the central canal remains double.

Section D-1 (fig. 9—D-1).—The level of this section indicated on fig. 8 is that of the fifth lumbar vertebra, and the position of the nerve roots show that it represents the second sacral segment of the cord. The cord is flattened antero-posteriorly; the central canal is double. Anterior horn cells are well developed; posterior horn cells cannot be distinguished. A small posterior column is present and is myelinated. The anterior and posterior nerve roots are myelinated. The cord contains little else that is recognizable; it is cedematous and broken up by fine vessels. The nerve roots of the cauda equina are disposed round it; those from the ribbon cord above are non-myelinated.

Section D-2.—Level of the third sacral segment, one millimetre below Section D-1. The central canal is still double at this level. Little change has occurred except that between this section and the preceding an adventitious septum of fibrous tissue has extended inward from the posterior pial sheath, and has here met and fused with the anterior median septum, completely bisecting the cord. Otherwise the structure is as before. In sections slightly below this level the fibrous septum once more disappears and the central canal is gradually lost on one side, so that the lower segments (fourth and fifth sacral) of the cord contain but one central canal which is placed slightly laterally.

Various explanations of this have suggested themselves to me. The simplest, and therefore perhaps the most probable, is that the mesoblast-forming pia which is seen in the upper portion of the myelocoele slightly elevated in the mid-line under the open medullary groove, has here likewise been abnormally elevated to a sufficient extent to cause bifurcation of the closing medullary tube. The mesoblast does not, however, come into relation

with the medullary plates in the normal embryo until these are already closed, but where one structure departs from the normal associated structures follow suit. Moreover, if the closure of the folds were markedly delayed in its relation to other processes, it is feasible that mesoblast would follow the time sequence of other mesoblastic development, and not that of ectoderm, i.e., medullary folds. A double central canal is not a very infrequent anomaly in cords with defects other than spina bifida.

GENERAL DISCUSSION OF CASE I.

Attention is especially directed to four features in this case, viz. :—

(1) The influence of the inequality of growth of cord and vertebrae, and the adherence of cord, producing abnormal direction of nerve roots and abnormal position of cord segments in the canal.

(2) The formation of spinal ganglia and nerve roots in segments in which closure of the tube has not occurred.

(3) The absence of histological differentiation in certain of the involved segments, and the normal histogenesis in other segments which are morphologically defective.

(4) The imperfect development of segments above the lesion due to mechanical hindrance.

CASE II.

Myelo-encephalocele—rachischisis completa totalis of Class 3 (B).

Specimen No. 1133, University of Texas Pathological Museum.

No complete account of the state of this specimen will be given in the present communication, but certain points in the spinal part of the defect are of value in the interpretation of the other cases under consideration. To these the description will be limited.

Description.—This specimen belongs to the general class of anencephalic monsters, of the type in which there is posterior cleft of the calvaria and spinal column. The mouth and nose are normal, the eyes bulge in the manner characteristic of this type of monstrosity; the forehead is low. The ears are normal in shape, but are situated close to the shoulders, and the chin is drawn down upon the sternum. This position is frequent in anencephalic monsters and indicates the absence or imperfect development of the cervical region, which is a usual accompaniment of the cranial and spinal defect. The general appearance of the body is otherwise normal, and the age about seven (intra-uterine) months.

The specimen shows posterior cranioschisis with protrusion of an imperfectly formed brain enclosed in a pia-arachnoid sheath; the dura covers the base of the skull and extends over the edge of the defect to blend with the skin of the anterior part of the head. The mass of brain tissue extends caudalwards and overlaps the upper part of the bifid spinal canal. Examination of the upper part of the spinal column shows that all the cervical vertebrae

are lacking, and the upper two thoracic vertebrae are either lacking or abortive, as are the cord segments corresponding to these. No attempt has been made at the present time to study the other defects of the cervical body segments. All the ten thoracic vertebrae which are present are cleft; the spinous processes and the laminae are normal in size, but flare outwards as do those in the affected area in Case I. Examination of the thoracic region shows that ten ribs are present, articulating normally with the thoracic vertebrae; and a cursory examination of the contents of the body cavities reveals nothing abnormal. The upper four lumbar vertebrae are flaring; the fifth has an incomplete arch, which is bridged by a fibrous band. The sacral vertebrae are defective in the spines only. The open vertebral groove is covered by meningeal layers from the base of the skull to the level of the fourth lumbar vertebra. At this level the meninges form a closed tube and pass into a zone of imperfect parchment skin, which blends at the level of the fibrous arch of the fifth lumbar vertebra with skin which is in all respects normal.

A ribbon cord similar to that described in Case I extends from the brain above to the level of the first lumbar vertebra below. Here it passes into a normal filum terminale which is prolonged under the meningeal layers into the sacral canal. The cord in a foetus of this age (seven months) should end at the level of the third lumbar vertebra. The slightly higher level assumed by this cord is apparently due to defective growth of its segments; it is greatly exaggerated in appearance in the undissected specimen because of the disproportion of the spinal column owing to absence of cervical segments. It is important to note that the entire cord is cleft; the coccygeal nerve arises, as do the nerves proximal to it, from a ribbon of medullary tissue. The lower nerve roots are grouped about the ribbon cord from which they arise, and pass under the meninges at the level of the fourth lumbar vertebra. Here the meningeal layers form a closed tube which passes under parchment skin as described above.

Discussion.—The features of this case which have a bearing on the anatomical characteristics of spina bifida restricta are the only ones to which attention is now called.

(1) The "upward migration" of a cord all the segments of which have failed to close.

This appears to be due to the absence of any abnormal adhesions between neural tube and surface ectoderm in this particular case. The formation of the filum terminale indicates that the adherence of the last coccygeal segment (rudimentary) has been normal.

(2) The formation of the lower vertebral segments, which has been retarded to a considerable extent after the upward migration of the corresponding open cord segments. The vertebral laminae should be formed in the eleventh week, while the migration of the cord does not take place until after the twelfth week. In the lumbar and sacral

regions, however, the completion of the vertebral arches is later than in the thoracic. In this case development progressed as soon as the ribbon cord slipped out of the way. This shows to some extent in Case I, but less strikingly because the complete cord defect in Case I does not extend below the second sacral segment, the segments below this being closed. In Case II, the entire neural tube is open, including the first coccygeal segment, i.e., the last segment which attains adult development in man. The fifth lumbar vertebra has, however, developed a fairly normal arch and the sacral vertebrae are deficient in spinous processes only.

The meninges attached to the lower segments of the open cord have been carried upward by the ascending cord, and the surface ectoderm has developed into normal skin over those vertebrae which possess reasonably normal arches, i.e., as high as the fifth lumbar.

These points will be found to throw light on certain obscure features of cases with defects restricted to the lumbo-sacral region.

CASE III.

Cystic myelocoele—rachischisis completa restricta of Class 3 (A).

History.—M. E., female, aged three months, John Sealy Hospital.

Family history negative as regards physical defects. This, the first child of this family, has been weakly since birth, and has had constant digestive disturbances. She appears to be normally developed except for a lumbar "meningocoele." Five days before admission to Sealy Hospital she had a febrile attack, which terminated three days later, when the upper part of the meningocoele ruptured. Pre-operative condition: Examination showed that there was a meningocoele occupying the lower lumbar and upper sacral region covered by typical parchment skin partially collapsed and ulcerated, of diameter of about one and a half inches. A minute opening was present at upper part, not in the mid-line, and from this cerebrospinal fluid flowed freely. There was no visible sign of nervous elements on the parchment surface, and the opening did not appear to be a central canal. There was, however, evidence that the condition was not confined to the membranes, as the legs were partially paralysed and there was incontinence of urine and faeces. In position of rest the legs were kept extended at hip and knee, and no movement of the feet were observed. The thighs were flexed feebly when the baby was disturbed. At the time of admission there was diarrhoea, but careful dressing and attention to cleanliness caused great improvement in the condition of the rectum and in the ulcerated surface of the meningocoele. Any handling of the child, and especially touching the sac, produced evacuation of the bowels and bladder. Complete collapse of the sac occurred from time to time, and at these times the child was restless and distressed. The flow of cere

fluid remained constant. Operation by Dr. J. E. Thompson, July 8, 1919, under ether anæsthesia. From the start the baby took the anæsthetic badly and artificial respiration had to be resorted to before the commencement of the operation. After this preliminary trouble, however, the respiration, though weak, was regular, and the heart fairly strong. A transverse incision was made and the sac opened. The filum terminale and a pair of nerve filaments were found to be spread over the lower extremity of its inner wall and these were removed with this portion of sac wall. Attached to the middle of the sac was the termination of the cord with its nerve trunks running down across the

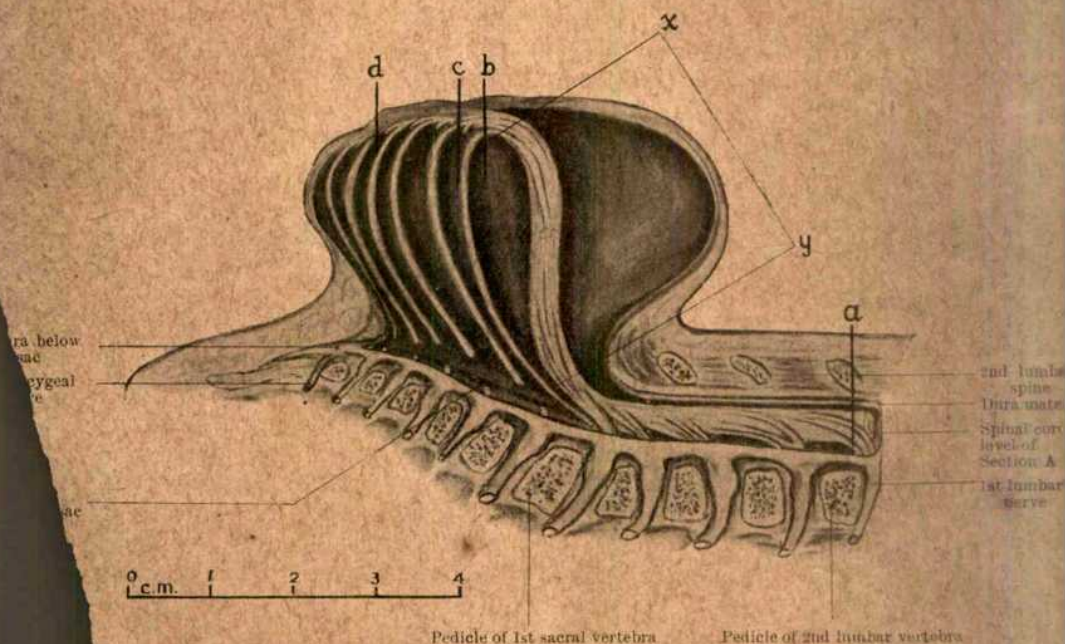


FIG. 10.—Case III, lumbo-sacral cystic myelocoele. Longitudinal section through vertebral spines; exposure of pedicles of vertebrae on right side; right nerve roots above lesion cut short; left sac wall and left roots within sac shown coursing across cavity. Drawing made from a composite of operative and post-mortem observations. Levels of microscopical sections indicated by letters a, b, c, d.

cyst into the foramina. This terminal portion of cord was cut across and the central canal found to be rather large, horseshoe-shaped and attached to but separated by the parchment skin of the sac. This was about the level of the first lumbar vertebra. Above and below this point the parchment skin merged with the normal skin of well-formed dura, which was dissected free on each side and the dura sutured over the cord with chromic gut stitches. The remaining parchment skin was dissected till normal skin was reached and this was sutured. The patient lay on the table in a serious condition of shock and within the next hour exhibited feeble convulsive movements of the whole body, including the legs

and feet. Death occurred within three and a half hours after the completion of the operation. Only a partial autopsy could be obtained and had to be limited to the affected area, so that observations on the condition of the internal organs and upper part of the central nervous system are unfortunately lacking. The lower four lumbar vertebrae, sacrum and coccyx, were removed in their entirety with the surrounding tissues.

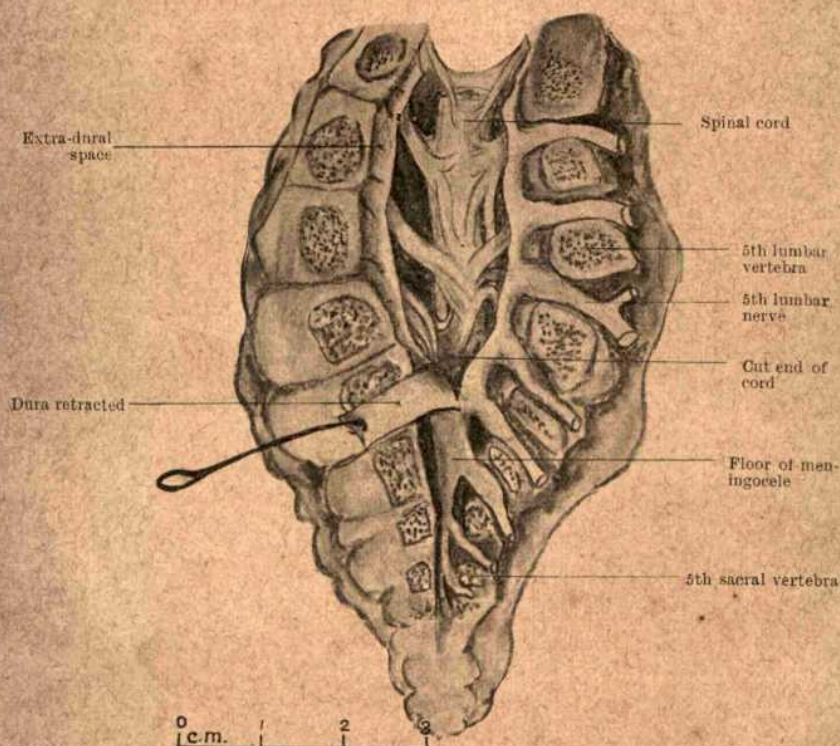


FIG. 11.—Case III, lumbo-sacral cystic myelocoele. Dissection of specimen as removed post mortem. Bodies of vertebrae split in anterior median line, exposing cord from its anterior aspect. On the left side the vertebrae have been further dissected to show the pedicles.

Description of myelocoele.—For the sake of clearness the description here given, like the accompanying diagram of the longitudinal section (fig. 10), will be a composite of operative and post-mortem observations. The sources of the information on each detail will be readily seen, but any attempt to separate the two sets of findings complicates the discussion unnecessarily. The laminae and spine of the second lumbar vertebra are normally developed. The pedicles and transverse processes of the vertebral arches of the fourth lumbar are normal, but the laminae and spinous processes of the fifth lumbar are absent, the vertebral foramen being closed dorsally by a dense fibrous band.

extending between the bases of the arches. The fifth lumbar has no such band, but presents a widely open foramen. The laminae and spines of all the sacral vertebrae are flaring and no fibrous band is developed.

Overlapping the third and fourth lumbar vertebrae, but not connected with them, is a thick meningeal sac which extends downward as far as the lower end of sacrum. This sac is covered by "parchment" of unusual thickness, which at the periphery is found to be composed of thin integument blending with a very dense dura, two or three times as thick as normal, which is in contact with a thin arachnoid. The subarachnoid space is filled with fluid. At the lower border of the fibrous neural arch of the fourth lumbar vertebra the meningeal layers of the sac are continuous with the sheath of the cord above, and the integument passes into the normal skin of the back. From beneath this fourth arch the cord emerges and passes dorsward through the sac, surrounded by small nerve roots which are held in close contact with it by the pia. At a point a little below the middle of the sac the end of the cord becomes attached to the inner surface of its dorsal wall, and lower down is inseparably blended with it. Near the mid-line of the sac the dura fuses with the skin, and cannot be lifted from it though it retains its characteristic shining inner surface. The pia cannot be followed by the naked eye below the point of attachment of the cord, but at its lower end it is considerably thickened, and just below this it fuses with the other meningeal layers. From this point down to the lower limit of the posterior wall (roof) of sac, these fused meningeal layers form a definite band of dense white fibrous tissue which projects into its cavity. This band is augmented by the nerve-roots which are carried down along the cord, and also, as will appear later, by some poorly developed cord tissue. It is possible that in the tense condition of the unruptured sac this thickened band would have been apparent from the external aspect, and might have served as a clue to cord attachment. Below and laterally to the point of attachment of the cord numerous nerve-roots are seen passing from the inner surface of the roof of the sac traversing the cavity toward the intervertebral foramina. The upper and larger of these nerve-roots pass freely across the cavity, but the lower smaller roots run caudward along the roof and then pass upwards a short distance on the floor of the sac in the substance of the arachnoid layer, which here is closely approximated to the dura. More careful study reveals the fact that those nerve-roots which arise from the saccular portion of the cord above its attachment to the sac wall, pass upward along the cord and enter foramina at a higher level than their point of origin.

In order to verify these observations, the anterior wall (floor) of the sac and that part of the cord above the lesion which had been removed after death, were exposed from in front by removing the bodies of the vertebrae. As is shown in the drawing of this dissection (fig. 11), not only the roots that arise from the intracistic part of the sac, but those which arise from the cord above the lesion, are found to course upward in the spinal canal before passing into their foramina. By a careful study of the relationships of the undivided

nerves above the operative section (B, in fig. 10) and of the divided nerves in the lower part of the sac, it is possible to determine that all the sacral roots and the coccygeal nerve were attached to the sac wall and were divided with it, and that the lower radicles of the fifth lumbar, as shown in fig. 10, were similarly adherent to the sac wall, but the upper radicles of this pair of nerves arose from the cord at some distance from its attachment to the sac, and passed up it to the foramina without interference from sac wall. Passing upward and examining the part of cord in the normal canal above the sac, one finds that the upward inclination of the roots decreases, but is still evident at the upper limit of the specimen, the roots from the level of the third lumbar vertebra passing through the twelfth thoracic foramen.

In fig. 11 it will be noticed that the nerve-roots exposed to view are somewhat curved owing to the relief of tension when the cord from which they arise was cut free from the sac wall at operation. This also accounts in part for the apparently small number and great thickness of the individual radicles as compared with the numerous delicate fibres found in normal cords. So soon as they have reached the floor of the sac the relationships of dura and of spinal ganglia and nerve trunks are entirely normal, and the anterior and posterior primary divisions of the sacral nerves pass through well formed foramina in the usual manner, though the position of the posterior foramina is obscured by the flaring vertebral laminae. It is evident, therefore, that the cord must have lain in contiguity with the vertebral rudiments when these structures, the roots and ganglia, were developing, as the normal connections could not have been established across a large cavity filled with fluid. The fluid collection in the subarachnoid space must, therefore, have occurred after these connections were made, and may be a result of the impairment of arachnoid function caused by the adhesions at the mid-line already mentioned.

The upward direction of the nerve roots to their foramina of exit is due to two factors. To one of these reference has already been made in discussing Case I; and attention is again called to fig. 5, in which the normal cord migration and its modification in Case I is represented. In the specimen now under consideration the first sacral segment of the cord was held in contact with the skin so that it could not slip upward in the spinal canal as this elongated. Consequently the cord between this point and the fixed first cervical segment was stretched to the full length of the enlarging canal. Were this the only force at work the stretching would have been uniform throughout the length of the cord and the nerve-roots would have continued to pass out horizontally to their respective body segments. However, the distension of the meningeal sac with fluid still further stretched the lower segments, so that they became actually longer than the spinal canal by the distance "x-y" indicated in fig. 10, and the nerve-roots above the point of cord attachment were carried below their foramina of exit to this extent, and so appear to ascend in the canal before emerging. This is shown diagrammatically in fig. 5, D.

The position of the roots below the adhesion of cord to sac is determined

by the same two factors, the fixation of the second sacral segment and tension by the sac, acting under different conditions. It must be remembered that in the normal migration of the cord, elongation of the roots takes place *pari passu* with the elongation of the canal, and the cord itself is never submitted to strain. In the meningocele, however, the tissues of the cord itself are stretched, and it seems possible that this may increase the minute histological defects found in these cases and so increase the amount of functional loss.

Microscopical examination.—Sections were made at the levels indicated in fig. 10. The region from the point of attachment of the cord to the end of the visible nervous tissue (*b* to *c* in the diagram), a distance of about four millimetres, was examined in serial sections, and those which are of the greatest interest are described. The transitional stages as illustrated in the intervening sections in the series are referred to between the descriptions of the separate sections photographed.

Section A.—Cord above the lesion (fig. 12, A): This was removed from the level of the second lumbar vertebra, but the relations of its nerve roots show that it represents the twelfth thoracic segment. The arrangement of the motor cells is not that of the lumbar enlargement. The shape of the cord in section is roughly pyriform, with the wide part anterior, and a depression on each side posterior to the anterior horn. The anterior median fissure is shallow, the anterior commissure normal. The central canal is narrow just above the septum, and posterior to this has two wing-like projections irregularly lined by ependyma. It then passes posteriorly and can be followed by means of its ependymal lining to within a short distance of the posterior surface. In the section photographed no posterior median septum is present, but in sections from the same block of tissue slightly proximal to this the central canal blends with a definite posterior glial septum. Anterior horn cells are few in number, but well developed; posterior horn cells cannot be identified with certainty, but a few nerve cells corresponding in shape and size with them are present in the region indicated in the photograph. The neuroglia in the whole section is loose in arrangement and oedematous, and contains an excess of small blood-vessels. Posterior nerve roots enter near the posterior mid-line; their ascending fibres form a small posterior column which is normally placed. Other myelinated fibres from these roots pass round the distorted central canal to end in relation to the cells of the posterior and the anterior horns. On the left side other myelinated fibres which have ascended for a short distance in the posterior column are seen passing round in the same manner to the cells of the grey horns.

Anteriorly there is a quite normal distribution of myelinated fibres representing tracts which cannot be definitely differentiated from one another in a normal cord of this age. The antero-lateral fasciculi are very prominent. An area of less definite myelination probably represents the lateral cerebro-spinal bundle. On the left side of the section there is a group of cells (*sub-gel.*), which probably correspond to the gelatinous substance. On the right side there is no similar group in this region but there is a less definite group in

relation to the entering fibres of the posterior root. It will be recalled that the gelatinous substance normally lies as a cap on the posterior horn, between it and the entering fibres. One or two myelinated fibres cross in the anterior commissure. There is an appearance of crossing fibres in the posterior commissure, but a careful reconstruction from the study of many sections from this area shows that these are fibres from the homolateral posterior column passing round the dilated central canal. The collapse of the central canal has caused a tear in the posterior part of the cord to the left of the median line, and the relations of structures in this region are much altered by the distortion. This has rendered the interpretation of the findings exceedingly difficult, but could not be avoided as it was the result of the operative procedure. In the uncollapsed specimen the central cavity must have been nearly circular, with its posterior wall composed of glia and nerve fibres and its anterior wall of the grey horns and anterior part of the white matter.

Section B (fig. 12, B).—This section is taken at the lower end of the cord, just before its attachment to the sac wall. The distribution of the nerve radicles from this shows that it represents the first sacral segment. Owing to the obliquity of the attachment to the sac wall the section shows a great enlargement of the cord in an antero-posterior direction. The transverse diameter is about normal. There is a well-marked anterior median fissure but no definite posterior median septum. The central canal is enormously enlarged and irregular in shape; its walls are collapsed as a result of the operation. The ependymal layer is present in the anterior portion of the cavity, but is lost posteriorly. This is the case in all the sections of this region, and appears not to be an artefact but to indicate a communication of central canal with an adventitious cavity.

In the substance of the medullary tissue are a few small collections of fluid, and the nervous elements present a loose arrangement, presenting evidence of oedema. There is in many places an apparent absence of nerve cells or fibres lying between the meshes of glial fibrils, and there are but few neuroglia or neuroblastic cells. Round the central canal there is a tendency for the cells to be spindle-shaped and to retain somewhat the type of the spongioblasts of the mantle layer of the embryonic cord. In the posterior region there is no trace of posterior horn cells, but posterior nerve-roots are myelinated and enter normally. In the anterior horn there is a well formed group of cornual cells of normal size, corresponding roughly in arrangement to those of lumbar enlargement, and the emerging motor fibres are myelinated and numerous, but somewhat irregularly grouped. The antero-lateral fasciculi proprii are myelinated and normally placed; no other tracts are distinguishable. The membrane covering this part of the cord is thicker than normal; and though laterally and anteriorly it appears to be composed of inflammatory pia only, posteriorly it blends with a dense layer which represents fused arachnoid and dura. Posteriorly also there is much leucocytic infiltration, probably due to the proximity of the inflamed sac wall.

Immediately below this section the cord was so firmly adherent to the sac

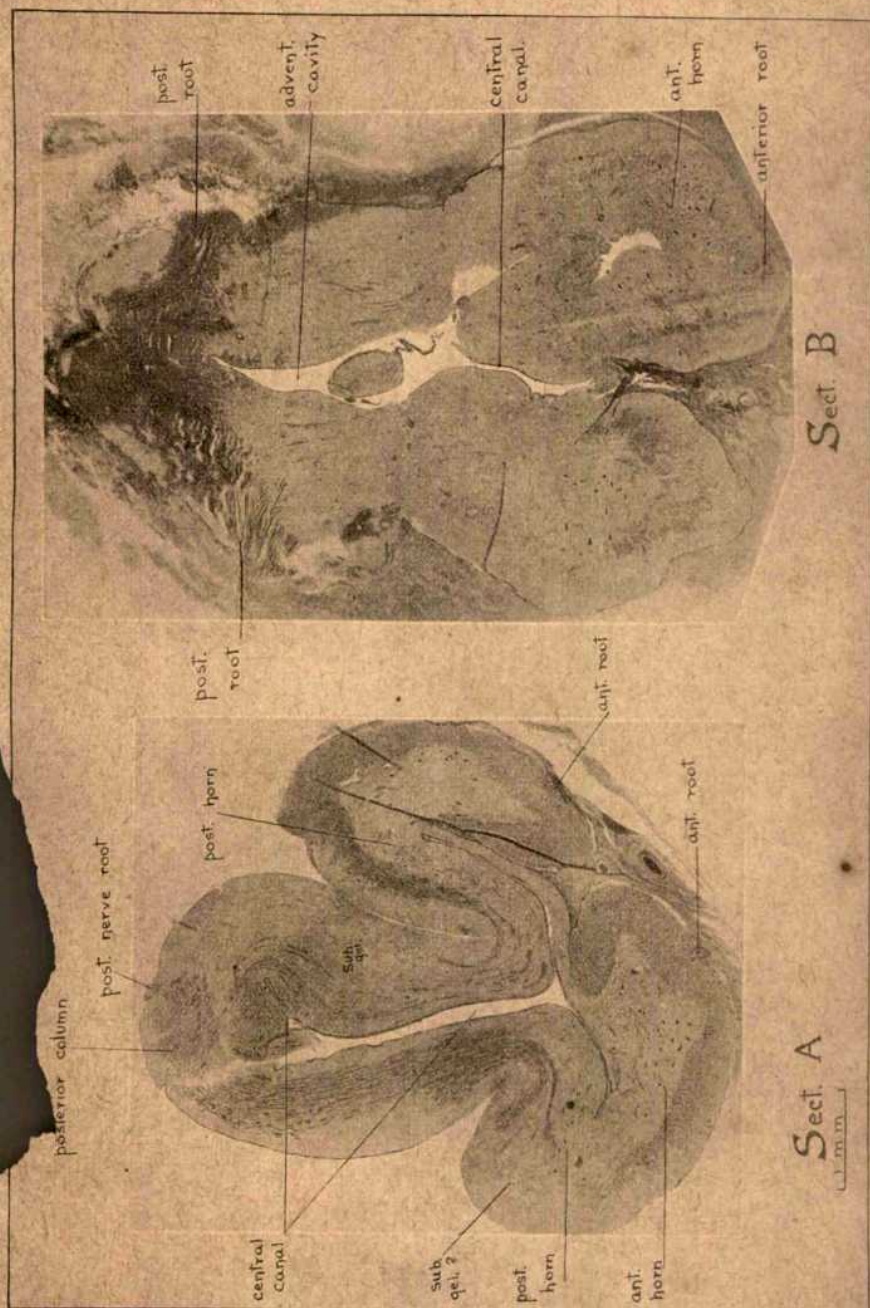
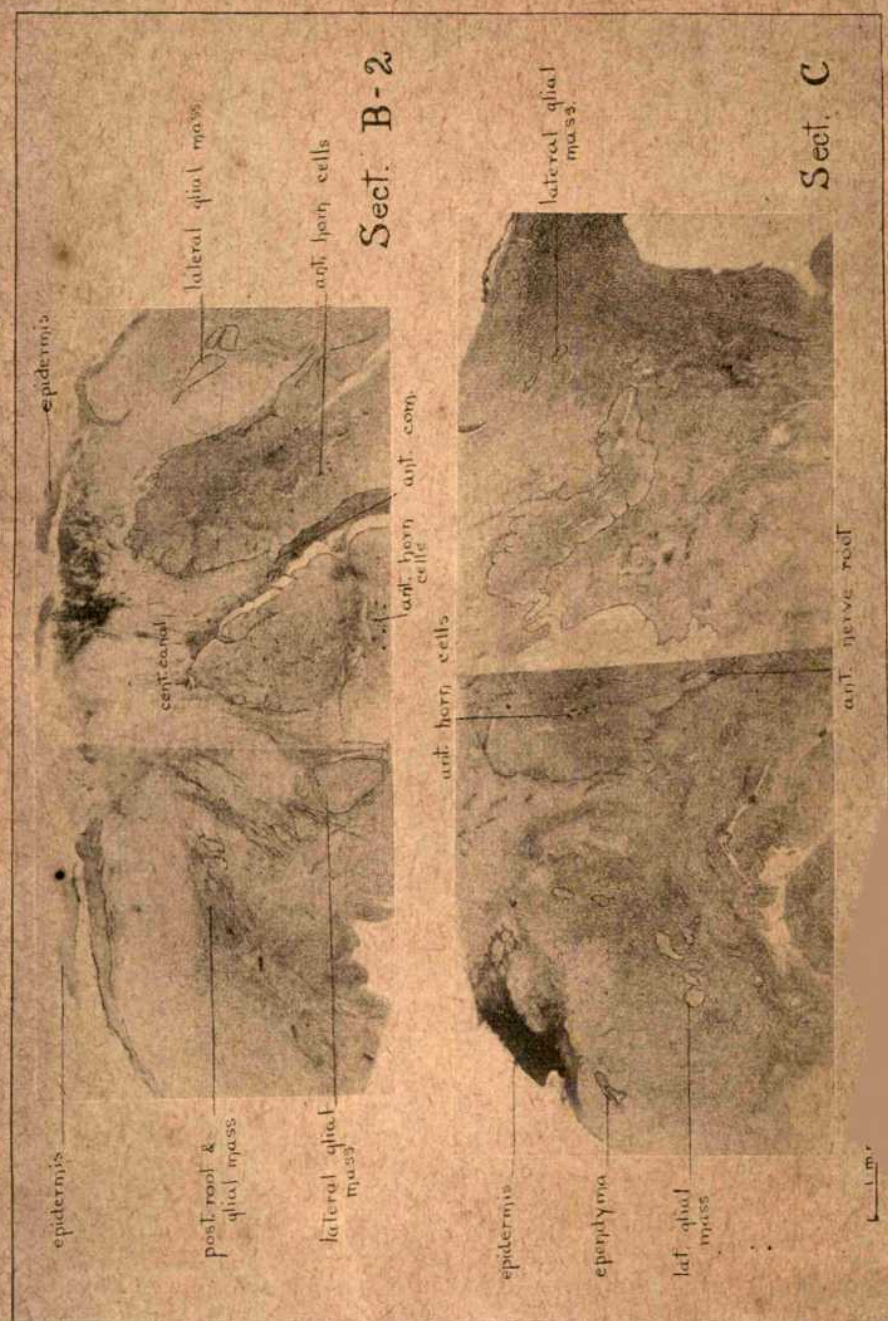


FIG. 12.—Case III, lumbosacral cystic myelocoele. Photomicrographs of Sections A and B at the levels indicated in fig. 10.



Photomicrographs of Sections B-2 and C, at the levels indicated in fig. 10.

wall that sections were made through this in order to preserve the posterior portion of the cord tissue. The first of the serial sections examined from this region (between B and C on fig. 10) shows that the posterior part of the cord is spread laterally as it becomes attached to the wall of the sac, and the adventitious cavity in Section B enlarges and approaches the surface. In the posterior attached portion less and less nervous differentiation remains, so that in the distal sections it appears only as a glial mass lying in the subcuticular connective tissue layer. This glial mass is separated into two parts by the extension of a fibrous band through the posterior median line towards the anterior median septum. In more distal sections this band of adhesions spreads into the posterior cord tissue laterally, and finally breaks it up into small, partly differentiated, neuro-epithelial masses. At the same time, the central canal persists in the anterior part of the cord but narrows as it approaches the posterior surface. The anterior median septum extends dorsally until it finally reaches and becomes fused with the subcuticular layer of fibrous tissue, thus separating the anterior portion of the cord into two lateral halves. In each of these a prolongation of the central canal persists for a time. In one of them it is carried somewhat more caudally than in the other. On account of the obliquity of the cord in this situation the interpretation of the sections is by no means easy.

Section B-2 (fig. 13).—The position of this section is half-way between B and E as indicated on fig. 10. There remains but little of the posterior part of the cord, and only in scattered masses close to the surface epithelium. At the median line the surface epithelium is thinned and in some sections absent, and beneath it there are many inflammatory cells in the fibrous tissue which separates it from the cord substance. The anterior part of the cord, recognized by a few motor cells, is separated into two halves by the adherence of the anterior median septum to the surface fibrous layer. The depth of this fibrous bridge and of the nervous tissue is increased by the obliquity of the section. At the point indicated in the photograph there remains the trace of the anterior commissure which persists for a few sections below this point and then disappears. No myelinated fibres are present except a few in the anterior part of the cord coming from anterior horn cells. The anterior roots and the extreme anterior part of the cord have been cut off by the removal of Section B. The posterior roots are non-myelinated and consist of but few nerve fibres with an excess of fibrous tissue; they lie close to the surface epithelium and are lost in the fibrous subcuticular layer before they reach the

At the left in the photograph (*cent. canal*) there remains a small epidural-lined cavity, the prolongation of the central cavity of higher sections. This is carried farther down on the left than on the right side. The nervous masses are connected with the thinned epidermis by strands of differentiated epithelium, infiltrated with inflammatory cells. The masses are considerably broken up by adventitious connective tissue and inflammatory material. The condition here recalls Case I, in which the cord passes into the closed distal segments. In

Case I, the transition is not obscured by adhesion to skin, and the bifid character of the central canal is more easily seen. In these the open segments are adherent to skin, and the relations are so altered that the stages are difficult to recognize.

Section C (fig. 13, C).—In this section the anterior part of the cord is still recognizable; one or two anterior horn cells are present in each lateral mass. On the left side an anterior nerve root emerges, but it contains no myelinated fibres, nor are there any in the anterior cord rudiments. Posteriorly irregular epithelial strands connect the nervous masses with the surface epithelium. (The loss of epithelium over the middle portion of the photograph is an artefact.) Laterally there are many small collections of partly differentiated neural epithelium, which appear to represent the posterior portion of the cord. On the left side one of these contains a cavity with a well developed ependymal lining, which has no connection with any other; it persists for but a few sections proximal and distal to this level.

In the remainder of the serial sections from this region the posterior (lateral) collections of neuro-epithelium become more and more attenuated and invaded by the surrounding fibrous tissue; the anterior masses remain recognizable for some distance, and are still present in the next section to be described.

Section D (not photographed).—At a distance of 10 mm. from Section C. The anterior masses are distinguished only by their position and relation to those in higher sections. No motor cells are present, yet nerve-roots approach close to the deep surface of the nervous tissue, and at certain points there appear to be emerging bundles of non-myelinated fibres. Between the integument and the neural masses there still persists an irregular and broken epithelial connection.

For a short distance below the last section nervous tissue is demonstrable and nerve bundles are present in the connective tissue to the caudal limit of the sac wall.

CASE IV.

Cystic myelocoele—rachischisis completa restricta of Class 3 (A).

History.—M. E. H., female, aged three weeks.

Father and mother healthy, except that mother has a "weak back," had no trouble while carrying child. Baby has one brother, aged 6, who had "infantile paralysis" at age of 1½ years, which has left his legs weak, though all the muscles seem to be equally developed. His sphincter control is normal. No examination of his back was made. No history of congenital defects in other members of either side of the family.

Description of condition.—Baby well formed, except for spinal defect. Nutrition good; no hydrocephalus apparent. In lower lumbar region a tumour size of half a mandarin orange, covered by parchment skin, protrudes on the surface and covered by a transparent dressing. On the tumour a small ulcerated area bleeds, but shows no purulent discharge.

Pressure near or on sac causes the baby to cry. Urination and defaecation occur frequently, especially when the child cries or the sac is touched. Movements of thigh are normal. In a position of rest the legs are kept straight, but passive plantar flexion causes slight active flexion of the knees. The feet lie in a position of flaccid semi-extension, and the usual "curl" of a baby's foot is absent. If the foot is irritated the extensors act so as to pull it into a position of dorsiflexion on the ankle, but the toes seem not to move. No response of any kind could be obtained to tickling sole of foot or pressing calf muscles. No attempt was made to determine the state of sensation in the thigh or perineum. Pre-operative diagnosis: meningocele; position of cord not determined unless indicated by ulceration of surface. Muscular responses probably indicate that the tibialis anterior (L. 4 and 5 and S. 1) and extensor longus digitorum (L. 4 and 5 and S. 1) are approximately normal. Peronei (L. 5 and S. 1) and small muscles of the foot (L. 5 and S. 1 and 2 and 3) are involved to some extent. Gastrocnemius and soleus (L. 5, S. 1 and 2); and the urethral and anal sphincters (S. 1 and 2, 3 and 4, Dejerine) are apparently completely paralysed. It seems probable that all the sacral nerves are affected; that the fifth lumbar is slightly so, and that the fourth lumbar is normal.

Operation by Dr. J. E. Thompson, October 30, 1920, under ether anaesthesia. Baby had irregular respiration from the time sac was opened until close of operation, but colour remained fair. Transverse incision. Parchment skin removed, cord found to be rather large at its termination, and to be attached to the sac at the middle where ulceration had taken place. The cord was cut free as close to sac as possible, and its end ligated. It was ovoid in shape and presented a rather large cavity. The level of its attachment was about opposite the fourth lumbar vertebra. Across the sac several large nerves coursed, and two of these on each side passed along cord to the roof of sac to which they were attached by delicate fibrous bands. These were separated, but it was thought that in cutting the cord at its attachment the roots of these were severed. One or two very fine nerve filaments were cut from the lower part of the sac roof below attachment of cord, which probably belonged to the lower sacral or coccygeal. It was impossible to separate these, and their roots had been necessarily cut with the end of cord. Dura and skin were separated at the side of sac and the wound closed in two layers, with a small gutter drain at one end under skin. Post-operative course, October 30, 1920: Condition remained good during day of operation, though the baby had one or two attacks in which the face became cyanotic, but the rest of body remained of good colour. Respiration appeared good during the attacks, which lasted fifteen or twenty seconds. These attacks continued to come more frequently and to be more severe, with irregular respiration. On November 1 the tube was removed from the wound, and was followed by considerable leakage of spinal fluid. This continued to drain profusely for some days, then became gradually less, but was still slight when baby was discharged. During the remainder of this day (November 1) baby took no nourishment; had twitch-

ings of the face and jerking of the eyes to the left (it was lying on the right side). These attacks of facial twitching became increasingly severe. They were at first accompanied by cyanosis, but this became less though the nervous phenomena increased. Attacks occurred whenever the child was disturbed or there was much noise. After an attack the baby seemed worn out, and would drop into a troubled sleep. On November 3 she seemed to regain strength, cried normally, and took some nourishment; but still had some attacks of facial twitching and slight cyanosis. Spinal fluid was draining freely from wound. November 4: had a severe attack of dyspnoea with twitching of the face, mouth, and eyes, and mild general convulsions. Attacks of this nature occurred frequently from 7 p.m. to 10 p.m., and then became less frequent and severe. November 5 and 6: had similar attacks, but of decreasing frequency and severity. On November 7 she had no severe attacks and was nursing better. Drainage from wound was slightly turbid and yellow for the first time. Similar discharge occurred for the next three days, after which there was only a slight drainage of clear cerebrospinal fluid. On November 11 "nervous attacks" ceased entirely, and from then on the baby's condition steadily improved. She left the hospital a few days later. Immediate operative result: No change could be seen in the muscular power so far as it could be determined after the operation. The nurse and the mother said that the big toe and the second toe were extended from time to time, but this was never observed by Dr. Thompson or the writer.

Description of the myelomeningocele.—In this case it is only possible to give the operative findings and the description of the sac as removed, so that all information regarding the cord above the lesion and accurate data regarding the relations of nerve roots and floor of sac are lacking. As viewed at operation, this case vividly recalled the appearance of Case III, and if the reader will refer to the diagram (fig. 10) of that case, the description of the conditions found in this case will be much more intelligible. The conditions found at the operation were: the end of the cord was rather large and distended with fluid, and attached to the sac at its mid-point, which in the distended condition of sac was thought to lie about opposite the fourth lumbar vertebra. Across the sac several large nerve roots passed, and two of these on each side ran along the cord, apparently attached with it to the roof of the sac. Below the attachment of cord one or two fine filaments were seen passing down from the roof of the sac to its floor; they were thought to represent the lowest sacral and possibly the coccygeal nerves.

Roof of sac: Immediately after the operation the removed area of sac was pinned out on cardboard, so as to preserve as nearly as possible its size and shape. It is very nearly circular, measuring $6\frac{1}{2}$ cm. by $6\frac{1}{2}$ cm. in the long and transverse diameters, and when seen from the posterior aspect (i.e., the external surface) all of this except a central area of about 5 mm. was found to be parchment skin, the peripheral area being covered by thin, fairly normal integument. The anterior aspect (fig. 14) is found to be clothed with a shining dura, which is inseparable from the surface layer, and within this is a delicate

arachnoid layer. Two and one-half centimetres below the upper limit of sac the cut end of the spinal cord is found, and from this point downwards, as is shown in the diagram, there extends a band of tissue 16 mm. in thickness at its broadest part, and narrowing slightly as it reaches the end of the sac. This band is irregular in shape, and somewhat hemorrhagic where it is continuous with the end of the cord, but below this region it is flat, shining, and rather sharply marked off from the remainder of the sac by two longitudinal bands of fibrous tissue. A vein which runs down the middle line of the band conforms in appearance with the anterior median vein of the cord. On the edge of the band the arachnoid appears to blend with the pial layer which covers it. Apparently the two lateral fibrous bands represent the ligamenta denticulata, but none of the lateral denticulations could be seen. In the upper portion

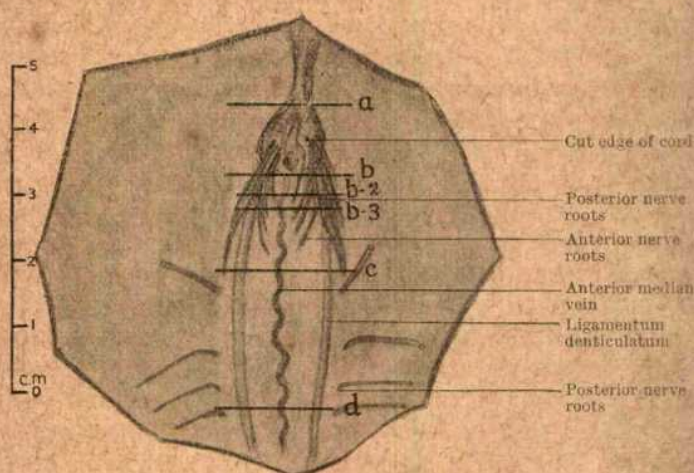


FIG. 14.—Case IV, lumbo-sacral cystic myelocoele. Interior of sac as removed at operation, showing band of altered cord tissue, and the region of cord attachment. Levels of microscopical sections indicated by letters a, b, c, d.

In the median band, medial to the ligamenta denticulata, it is possible to find a few delicate nerve filaments representing anterior roots proceeding outward and upward on the sac roof, and apparently cut off with the end of the cord. These cannot be found in the caudal 25 mm. of the band. Lateral to the ligaments, nerve filaments (posterior roots) can be found lower down, to within 25 mm. of the end of sac. These filaments are very delicate and lie free in the sac; they do not arise from the cord above, but directly from the band of tissue just described. If the inference drawn at operation be correct, that the two roots are the fifth sacral and coccygeal nerves, by counting back from the point of attachment it would be possible to determine with more or less accuracy the segment attached to the sac. This is probably the first sacral or fifth coccygeal. The clinical examination appears to corroborate this. The presence

of these nerve roots would lead one to expect to find nervous tissue in the median band as low down as the last pair of roots, but by the naked eye nothing resembling normal cord tissue can be seen below the point where the cord has been cut obliquely free from the sac wall. A section immediately below this point, through the sac roof, shows a soft cystic friable mass of tissue, and sections below this reveal only a pink, soft mass of tissue, slightly thicker than the rest of the sac wall, extending laterally a little farther than the band of tissue described on the inner surface, but having no resemblance to cord tissue. As will be seen, however, the microscopic examination of sections through this region are not disappointing.

Microscopical examination.—The sections described were made at the levels indicated in fig. 14, through the median band. The end of the cord had been severed by the operative procedure so close to the sac wall that no section of it could be made before its attachment to sac. At its point of attachment serial sections of the entire region were made, and the photographs are selected from these. The area so examined extended from A to C in the diagram; the changes observed in intervening sections of the series are noted between the descriptions of the individual sections.

Section A (fig. 15).—This was taken proximal to the point of cord attachment, but the lower sections of the block show a small part of the cut surface of the cord. The surface is covered by thin, stratified, cornified epithelium, below which is a dense layer of connective tissue, representing fused corium and dura. Below this laterally is a thin layer of connective tissue covered by endothelium, the arachnoid, which, thickening as it nears the mid-line, becomes blended with the pia and lies in direct relation to the posterior part of cord tissue. The upper limit of the adherent portion of cord is here seen represented by a mass of glia, in which no nerve cells nor myelinated fibres are present. The anterior part had been cut away in the operation.

Section B (fig. 15, B).—This section is taken immediately distal to the point of cord attachment, and is the first of the series through the region which has not been affected by the operative incision. It is probable that it represents the first sacral segment of the cord (cf. gross description). As will be seen in the photograph, the surface here is covered by a thin layer of stratified squamous epithelium, imperfectly cornified, and having none of the normal skin glands nor papillæ. Immediately below it is a mass of connective tissue which is in parts densely infiltrated with leucocytes and with blood.

Below this layer of connective tissue there is a dilated cystic cord, of which the anterior portion only bears any resemblance to normal cord structure. Laterally the subcutaneous connective tissue is found to blend with an imperforate dural and arachnoid layer, but in the region where nervous tissue exists they are not present. The cord anteriorly is clothed by a thick layer of vascular connective tissue, apparently a thickened outer layer of pia mater in which the nerve roots; and within this is a delicate connective tissue membrane which appears to represent the inner layer of the pia. Both these layers are continuous posteriorly in the subcutaneous connective tissue layer already mentioned.

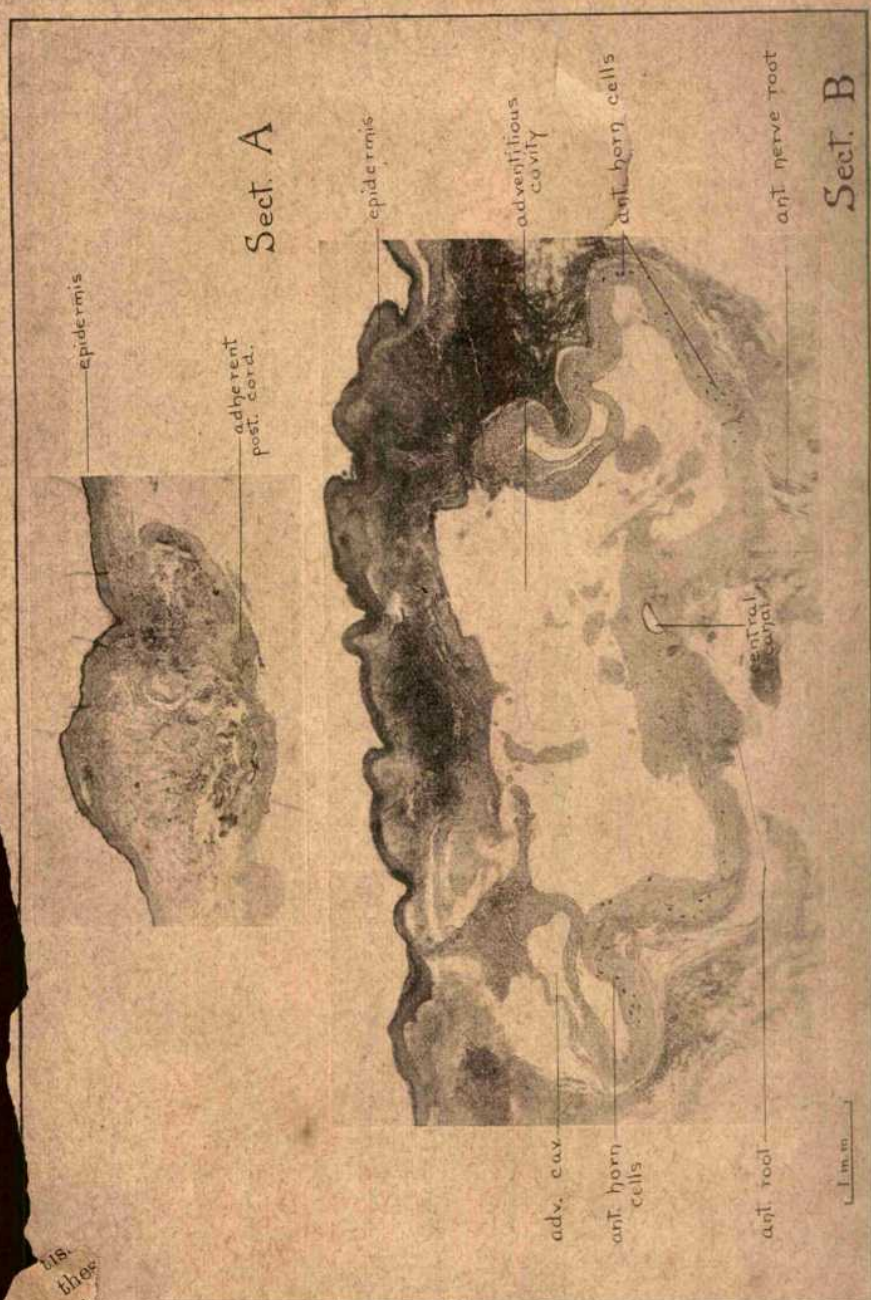


FIG. 15.—Case IV, lumbosacral cystic myelocle. Photomicrographs of Sections A and B at the levels indicated in fig. 14.

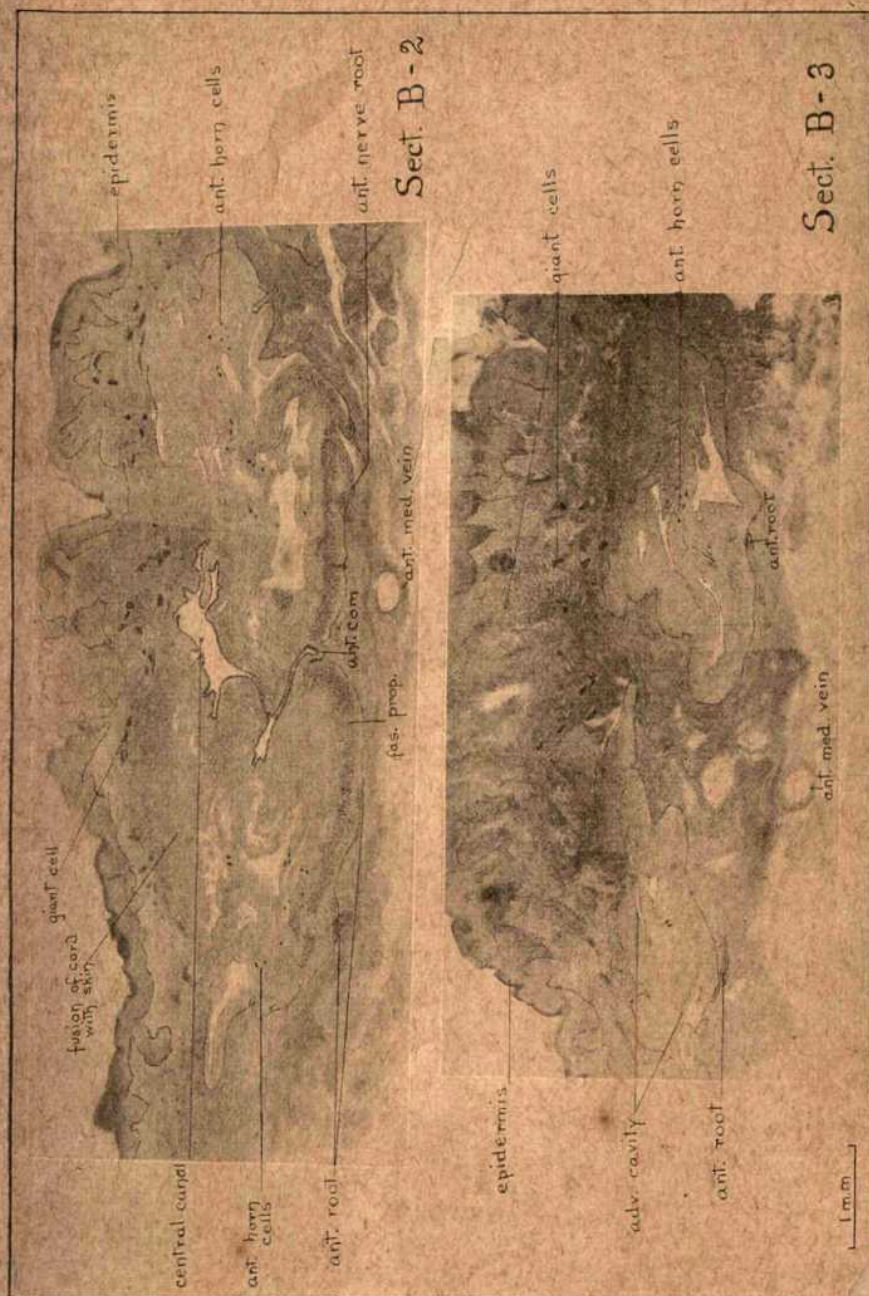


Fig. 14. Photomicrographs of Sections B-2 and B-3 at the levels indicated in fig. 14.

The most striking feature in the cord is a large, irregularly-shaped fluid-filled cavity, which in the section is much distorted by the operative procedure. This is not a dilated central canal; it is not lined by any membrane, but by the neuroglia of cord substance. Posteriorly on each side is a smaller cavity, separate from the main cyst, which in the light of observations on other cases may possibly represent the position of undeveloped posterior columns. No trace of the posterior horns or columns can be found, but there is an irregular mass of neuroglia on each side. Toward the mid-line these masses are lacking, and the cavity in the cord tissue is bounded by the subcutaneous connective tissue layer. Anteriorly there is a well-formed, ependyma-lined central canal, and on either side of this well-formed anterior horn cells can be found, irregularly grouped along the anterior wall of the cystic cavity. Myelinated fibres are seen to pass from these and to emerge as fairly large anterior nerve roots. There are also numerous myelinated fibres forming a marginal zone over all the anterior half of the cord; these are probably all association fibres.

In the connective tissue surrounding the cord the nerve bundles are found arranged in two groups; one of these lies anterior to the cord in the mid-line, and then passes outwards to the sac wall. Into this group the anterior root fibres may be seen to pass from the cord. The other group lies close to the surface epithelium, and none of the fasciculi can be traced to the cord. It appears that the fibres in this second group represent the posterior roots approaching the cord from the spinal ganglia, but they never reach it, otherwise some should have been found in the great number of sections examined. This presupposes the proper development of the spinal ganglia, which is not owing to the circumstances of the case capable of proof. As has been seen, however, in the discussion of Cases I and II, the spinal ganglia sometimes develop even in cases with more marked neural tube defects than are here present, and the relationships of these fibres placed posteriorly to ligamentum denticulatum, makes it reasonably certain that they represent posterior roots. Between Sections B and C the cyst rapidly narrows. Microscopically the small central canal which is present in Section B enlarges posteriorly, and gradually assumes the proportions seen in the next section. It does not, however, communicate with the adventitious posterior cavity, but extends dorsally until it comes in contact with the subcuticular fibrous layer, and thus separates the adventitious cavity into two.

Section B-2.—Three millimetres below Section B (fig. 16—B-2). The most striking feature of this section is the huge central cavity which abuts directly against the subcuticular fibrous layer without the intervention of any nervous tissue. Its ependyma is unbroken, and the irregularity of shape is due to collapse of the wall in preparation. On either side the adventitious cavity seen in Section B is similarly collapsed and is broken up into smaller compartments. The anterior median fissure is shallow, and the anterior commissure hardly discernible. Anterior horn cells are still present but are few in

There are a few myelinated fibres in relation to the anterior horn in the region of the antero-lateral fasciculus proprius, but the anterior

roots, which are found in the region indicated in the photograph, are largely non-myelinated. All the rest of the nervous tissue is composed of undifferentiated glia and possibly unmyelinated fibres.

In the following sections of the series the central canal becomes smaller, first anteriorly, and in lower sections posteriorly also, and the anterior median fibrous septum passes more and more dorsally until at the point where the central canal disappears entirely the nervous tissue is separated into two halves by the fusion of the anterior median septum with the fibrous subcuticular layer.

Section B-3.—Two millimetres below Section B (fig. 16—B-3). In this section one or two anterior horn cells may still be found. The nervous tissue is separated into two masses by a thick septum of fibrous tissue which extends dorsally to the subcutaneous tissue; in each of these irregular adventitious cavities are present, the continuation of those seen in higher sections. One or two anterior horn cells are present; but the remainder of the nervous masses, composed of glia and possibly unmyelinated fibres, can hardly be recognized as cord tissue. Between the surface epithelium, which is partly destroyed in the median line by ulceration, and the nervous tissue, a small number of giant cells are present and a few irregular epithelial strands.

Distal to this section the nervous masses become more and more indistinct, and about one millimetre below this level the appearance is exactly similar to that in Section C, though this is taken at a lower plane.

Section C (not photographed).—Through the median band, 11 mm. below Section B (fig. 14), 6 mm. below Section B-3. Laterally the character of the surface epithelium, connective tissue and meningeal layers is precisely like that in Section A. In the middle 10 mm. of the section, however, the surface epithelial layer loses its stratification, and merges into a mass of ulcerated imperfectly differentiated epithelium of considerable thickness, which is ulcerated and forms the bulk of the section in this region. Many small blood-vessels course through this mass, and its deeper layers are crossed by transverse bundles of fibrous tissue. Deeper down it is rather sharply limited by a connective tissue layer corresponding in appearance with the pial layer in the preceding sections. Between this and the more superficial connective tissue are irregular masses of epithelium of embryonal appearance, some of which are clearly neuro-epithelium.

Scattered through the epithelial masses are many irregularly shaped giant cells, such as are found in the two preceding sections. Some are of great size and contain large numbers of irregularly disposed nuclei. They do not conform to the type of the usual foreign body giant cell, and are difficult to explain. None are found beneath the pia. Probably they are endothelial in origin and may represent imperfect budding capillaries. The elongation of some of the larger cells, and the presence of red blood cells in one or two, seem to bear this out.

Section D (not photographed).—This section is taken 14 mm. below Section C, at a point where the thickened median band begins to thin out.

end of the sac. It shows the surface and meningeal layers already described in Section A, and is of interest only because of the absence of the giant cells seen in the last section, and because laterally it possesses medullated nerve fibres, though it contains no cord elements. These are the posterior roots described and shown in fig. 14. The examination of sections between this and Section C shows that they do not pass up to the well-formed cord above, but are lost in the fibrous tissue.

CASE V.

Hydromyelo-cystocele—rachischisis completa restricta of Class 3, A.
Specimen No. 77, University of Texas Pathological Museum (1893).

History.—The baby had been admitted to hospital at the age of 1 year for treatment of a lumbo-sacral meningocele. Following the injection of Morton's fluid, then in use (1893), the baby promptly died. No facts regarding muscular power are available; the baby had double congenital talipes equino-varus.

Description of specimen (fig. 17).—All the lumbar and sacral vertebrae had been removed with the tumour, bisected along the mid-ventral line and spread apart so as to expose the cord and the floor of the tumour from in front. Posteriorly the greater part of the right wall of the meningeal sac has been dissected away so as to expose its interior.

The upper three lumbar vertebrae are normal; the spine of the fourth lumbar vertebra is slightly smaller than normal; the fifth lumbar is cleft, its laminae and spines flaring outwards. The columns of the sacro-spinalis muscle spread outward also so as to obtain attachment to the flaring spines. All the sacral vertebrae are bifid; but while the spines of the upper three flare, those of the last two are not more widely separated than in the normal sacrum. Through the opening in the spinal canal, the meninges and cord pass dorsalward. The meninges are adherent to skin and form a large sac, to the middle of which the cord is attached. It measures 4 cm. in antero-posterior and $3\frac{1}{2}$ cm. in vertical diameter, but shows evidence of shrinkage during fixation. The skin covering it is fairly thick and has the appearance of normal integument, but section shows that it is without a fatty layer, and that its inner surface is inseparably fused with the dural layer of the sac. The further study of the sac will be simplified by reference to the drawing (fig. 17) which was made from the specimen and reproduces as nearly as possible the results of dissection. The only feature in which it is diagrammatic is that the cord is represented in longitudinal section throughout the whole of its upper portion, and the central canal as greatly enlarged. This was not visible to the naked eye in the dissection because of the collapse of the walls of the cord from the point B in the drawing, to the upper end of the cord in the normal canal; the dilatation is, however, easily demonstrable in sections at various levels. This may be more fully explained later.

Under the fourth lumbar arch the cord passes dorsalward at a sharp angle

to the roof of the sac, where it flattens out and adheres to the middle of its roof. Above its point of attachment a fairly strong connective tissue septum extends downward from the sac roof to the lateral surface of the cord, where it blends with the pia. Where the cord passes into the normal canal above, i.e., at the "neck" of the sac, this septum is very narrow and fuses on the ventral side with the pia around the cord and on the other with the dura mater of the sac wall. In the dissection only the left side of the cord

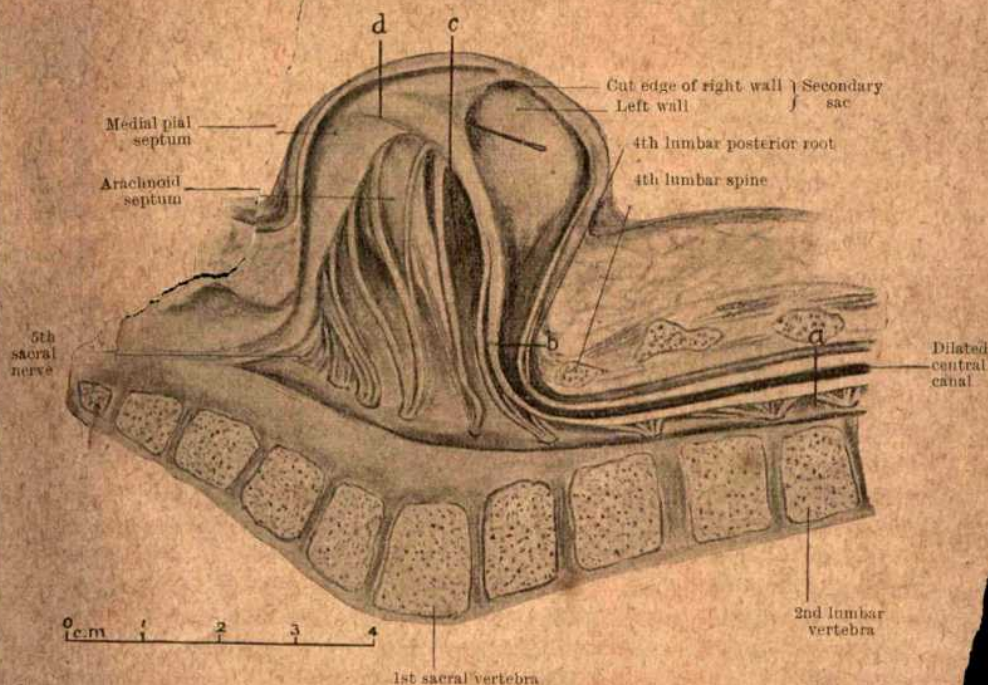


FIG. 17.—Case V, lumbo-sacral cystic hydromyelocele. Longitudinal section through sac as removed at autopsy. Cord had collapsed as result of a fixation from the point b upwards, and is represented in its dilated condition. In all other respects the drawing accurately reproduces the condition of the preserved specimen. A probe is passed into the right lateral pocket of the dilated cord cavity. Levels of microscopical sections indicated by letters a, b, c, d.

shows this septum, but along its right aspect there is evidence that a similar septum had been cut away, and that in the original condition the cord was slung between these two. On examining the posterior portion of the cord between the septa, it is found to be degenerated and to bear no posterior root fibres. Where the cord emerges from the canal and enters the sacral nerve roots may be seen to pass from its posterior surface and to blend with the upper part of the roof of the sac as shown in the diagram. The anterior surface of the cord appears to be normal and its nerve roots

and course forwards toward their foramina. It seemed probable from the dissection that the septa just described had enclosed within them the dilated posterior part of the cord, and further study proved this to be the case. The preservation of the sac wall had not been sufficiently good for any nervous elements to remain uninjured in the exposed region where the right septum had been dissected away. It is found, however, that where the end of the cord joins the sac wall it is much flattened and that the secondary sac just described passes into two lateral pockets. One of these, the right, is shown in the drawing with a probe passing into its depths. These pockets terminate close to the lateral masses of the cord tissue below, and, as will be seen later, they are lined by ependymal cells. Moreover, at the point B in the diagram, where the cord in the preserved specimen is small and flattened, section shows that its walls are thin and fluted, indicating that it had been greatly distended with fluid. Higher up in the normal canal the cord appears flattened in an antero-posterior direction, and here also gross and microscopic section shows that there has been collapse of a large interior cavity. This and other microscopical observations prove that the secondary sac consists of a cyst of the dorsal part of the cord, surrounded by pia and adherent to the sac surface, and it is so represented in the diagram.

Distal to the attachment of the cord, another delicate septum extends like a veil about half-way through the depths of the sac, and laterally on the left side (the right has been dissected away) is another septum which terminates in the sac wall. The relationships of the nerve-roots to these septa and the lateral veil is pial and the lateral is arachnoid.

In the drawing, the lower part of the sac is traversed by many roots, some medial to the arachnoid septum and lateral to the other, and are more or less entangled in delicate fibrous tissue. The last roots which emerge from the sac, before its attachment to the sac roof, are the fifth and sixth. The anterior radicles come from the cord, and the posterior from the sac wall where it is adherent to the posterior cystic part. The roots are fairly large, but not so large as those in a normal sac. They are divided into two groups, anterior and posterior, and pass in a usual manner and pass into foramina in the floor of the sac. The posterior roots, however, appear to join any normal cord tissue on the roof of the sac, but to come directly from the sac wall at a point below the demonstrable cord. It was not possible to dissect these after they became adherent to the roof of the sac, as they are fused with the dense tissue of its dural lining.

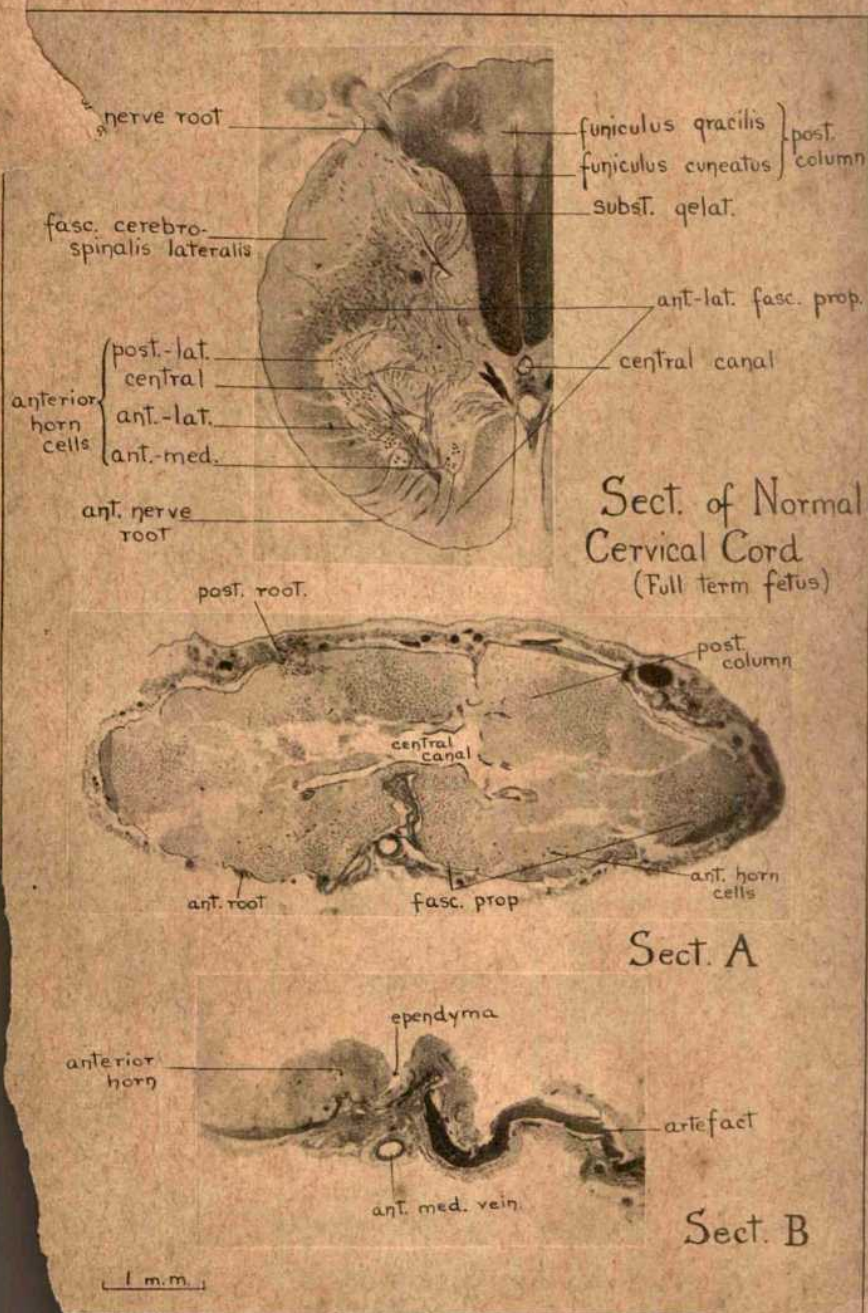
The arrangement of the roots above the lesion is, perhaps, sufficiently clear from a study of the diagram alone, since it is in no way different in principle from that found in Cases III and IV, of which full explanation was given.

Microscopical examination (figs. 18 and 19).—Sections were made at the points indicated in fig. 17. In spite of the age of the specimen the staining with haematoxylin was very satisfactory, though the other stains were less successful. The only serious difficulty was that the tissues were so friable

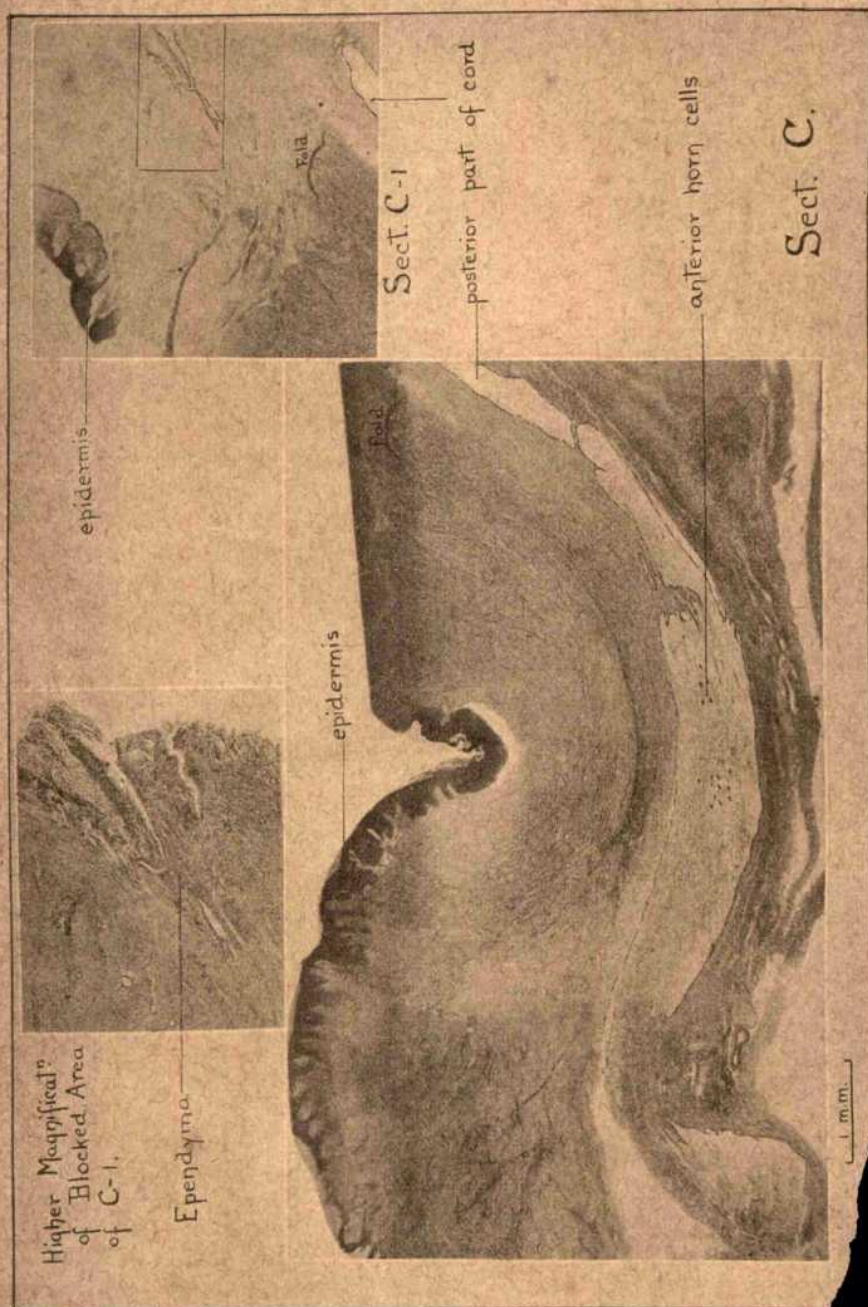
that it was difficult to cut blocks for examination without tearing the sections. This was especially true of the dilated cord as it entered the sac. In the removal of the right myelocoele wall the pia had been incised, and when Section B was cut its walls spread into a long thin ribbon of tissue, and lost their circular conformation. The examination of the sections was, as a whole, much more instructive than one would expect after so long a time in preservatives.

Section A (fig. 18).—Level of the second lumbar vertebra, above the lesion. The foramina through which the nerve-roots pass indicate that this is the first lumbar segment of the cord. The shape of the section is flat, as the result of the escape of fluid from its interior, owing to tearing of the pia. The anterior median fissure is normal; in the posterior median line a small fibrous septum composed of pia extends inwards almost to the central canal, from which it is separated by a glial commissure connecting the two halves of the cord. In sections at the upper part of this block of tissue, 1 mm. above the section photographed, this adventitious pial septum disappears, and the posterior glial septum is normal. It therefore represents the beginning of the abnormal adherence between the posterior wall of cord and the meninges, which is so much more intimate lower down. The central canal is very large and flattened antero-posteriorly, due to the escape of fluid. Anterior horn cells are well formed though few in number, but it must be remembered that the cord was pulled out by traction from the sac below, so that the cells in a given section would be less numerous than when the tissue was normally concentrated; and the total number of cells in each segment is not necessarily reduced. In certain of the sections from this area anterior nerve-roots emerge in the region indicated in the photograph. Posterior horn cells cannot be distinguished; the position of entering posterior root fibres is shown. Myelinated posterior columns are present, and there appears to be a small lateral cerebro-spinal tract and a number of other myelinated fibres, some of which may represent descending tracts. They are not sufficiently well differentiated to name them with accuracy; probably many belong to the fasciculi proprii. The median part of the posterior column, usually occupied by the long fibres from the posterior roots, contains less myelinated fibres than the lateral part. This part is composed of the lower of the ascending posterior root fibres, and in this specimen many of these are caught in the meningeal sac and never reach the cord. Throughout the section there is a preponderance of glia cells and a considerable number of lymphocytes.

Section B (fig. 18, B).—Dilated cord just below its entrance into the sac. The nerve roots which originate here pass into the fourth lumbar foramen so that this represents the fourth lumbar cord segment. The cord here is contracted into a flat, narrow band, but when the section was cut it stretched widely, so that it was evident that it had been greatly distended with fluid. The attempt to preserve its circular form was a failure and the photograph shows only a small portion of the anterior region. The pia over all the surface is thickened, and posteriorly it blends with a dense dura-arachnoid.



18.—Case V, lumbo-sacral cystic hydromyelocele. Photomicrographs of sections made at levels indicated in fig. 17. Upper section is from a normal cervical cord (full term fetus) for comparison, under the same magnification as other photographs.



Photomicrographs of Section C, made at level indicated in fig. 17. Fold in section coincides with that in Section C.

of which are indistinguishable and infiltrated with inflammatory cells. This dural layer blends posteriorly with the subcutaneous fat in the neck of the meningocele. The anterior mid-line is indicated by a short prolongation of the pial layer inward and a large anterior median vein, but there is no true anterior median septum. Near this many bundles of myelinated nerve fibres (anterior roots) are found lying in the pia where it blends with the dura of the sac. Emerging anterior root fibres are found near the median line, but posterior roots could not be seen entering the cord. Within the pia there is a small layer of nervous tissue. This is somewhat thicker near the anterior median line, and in this region there is a diverticulum from the general cavity which appears to be imperfectly lined by ependymal cells. On either side of the median line there are a number of vacuolated cells with pale nuclei, which possibly may be anterior horn cells which have undergone degenerative changes. No other nerve-cells are present; the layer of tissue is an indiscriminate mixture of partly myelinated fibres and neuroglia with a few small vessels and occasional lymphocytes, but with no landmarks by which one can recognize even its regions with accuracy. Except for the few doubtful ependymal cells mentioned above the central cavity is without definite lining, and is bounded by the degenerated nervous mass which has been described. It is impossible from this section, therefore, to say whether the cyst is a dilated central canal or an adventitious cavity, though it seems probable from the sections above and below that it is a dilatation of the central canal.

Section C (fig. 12, C).—Wall of sac and attached end of the cord, with the lateral pocket of the hydro-myelocele. The nerve-roots from this portion of the cord are those of the first sacral nerve, indicating that this represents the first sacral segment of the cord.

The surface epithelium is fairly thick and has a few papillary processes; hair follicles and skin glands are lacking, as is the subcutaneous fatty layer. Beneath the epithelium are dense bands of fibrous tissue, the fibres of which run transversely to the long axis of the cord. Below this fibrous layer is a layer of looser, more delicate connective tissue, considerably infiltrated with round and polynuclear cells. Laterally this layer extends about 5 mm. from the middle line, and there splits into two leaves, of which one passes laterally to merge with the dura-arachnoid lining of the sac. The other passes medially, and with the corresponding leaf of the opposite side forms a sheath for the attached end of the cord. The whole of this layer, which represents pia, is densely infiltrated with inflammatory cells. At the middle line the anterior folds project upwards towards the roof of the sac, forming an imperfect anterior median fissure in which the pia is distinguished by its great vascularity. The cord tissue enclosed between the layers of this pial sheath bears the resemblance to normal cord. The inflammatory connective tissue which closes the gap between anterior median septum and sac roof divides the nervous tissue into two masses; no nervous elements can be recognized crossing these across the median line. No trace of central canal is present. In the nervous mass certain structures can be determined. The

photograph (fig. 19, C) shows but one lateral half and a very small portion of the other, with the median anterior septal mass of connective tissue already described. It will be seen that the cord is not rounded, but is represented by a flattened band, each half of which is roughly divided into two regions. In the more medial of these anterior horn cells normal in size and shape are easily recognized. Lying between them are many glia cells, and many fibroblasts and inflammatory cells. In the more lateral of the nervous masses no nerve cells can be distinguished, the mass consisting of glia infiltrated with a few inflammatory cells. No myelinated fibres can be found in any portion of the cord tissue, save one or two delicate scattered fibres in the region of the anterior horn cells. In certain of the sections from this region anterior root fibres emerge in the position indicated in the photograph. No posterior root fibres can be found entering the cord tissue.

Passing laterally to the outer limit of the posterior region of the cord (i.e., the lateral glial masses), separated from these by the fused dura-arachnoid lining the interior of the sac, and lying near the integumentary epithelium but separated from it by connective tissue, is the lateral pocket of the dilated proximal portion of cord. (Of fig. 17, in which a probe is passed into this pocket, and the description of the gross findings.) This pocket is shown in C-1 on fig. 19. It is lined with a perfect layer of ependymal cells, surrounded by a narrow zone of glial cells, among which there are a few myelinated fibres. In the more distal sections from this block the pocket ends blindly in a small glial mass; it never makes any direct connection with the lateral cord masses at this level. As one passes caudalwards from the end of the cord the sections show the same general characteristics, but the anterior horn mass becomes less definite, and the lateral (posterior) masses are separated into smaller portions by strands of connective tissue. They spread also more laterally, and 2 mm. distal to the section shown in the photograph are so attenuated and mingled with connective tissue that little neural character remains.

Section D (not photographed).—Taken 5 mm. below the level of the block cut for Section C, through the wall of the sac where cord tissue has apparently blended with it.

Here there are a few imperfect hair follicles and sweat glands; no subcutaneous fat is present. The tissue below the epithelial layer is denser connective tissue than is normal, and towards the interior of the sac it blends with the dura arachnoid and with an imperfectly differentiated pia, between the layers of which are nerve bundles. These are numerous and conspicuous, but examination shows that they contain but few myelinated fibres. The nerve roots seen by the naked eye is therefore misleading. A small glial mass is found at the median line, but this contains no true nerve cells or central canal. The surface epithelium immediately above this glial mass shows an unusually deep slender papillary process of elongated spindle-shaped cells; but no connection between this and the glial cord mass can be demonstrated, as they are separated by but a thin layer of connective tissue.

GENERAL DISCUSSION OF CASES III, IV, AND V.

The points of interest in these three cases are discussed together because clinically and anatomically they are closely allied.

(1) The lesion in all is lumbo-sacral and had the clinical appearance of a pure meningocele, though in two of the cases ulceration of the sac wall might have led to a suspicion of involvement of the cord.

(2) In each the cord is bound to the wall of the sac by the segment corresponding to the highest vertebral segment which is cleft.

(3) The collection of fluid has drawn the cord above the proximal affected segment down into the sac, so that higher segments are influenced by traction.

(4) Hydromyelia in cord segments above the lesion is present in each case, extending as high up as the cord was removed at autopsy in two cases and as high as it could be observed at operation in the case without autopsy, and for an unknown distance above this. In Case V this is most marked and is complicated by the adherence of the intrasacral portion of the cord to the sac wall, causing a secondary myelocystocele.

(5) The cord at the level of the point of attachment in each case is cut off from both ascending and descending nervous connections by the adherence of cord tissue and nerve roots to the sac wall, so that even before operative interference the lesion amounted to an almost complete transverse lesion of the cord at this point.

(6) Segments of the cord lying distal to the segment attached to the sac are imperfectly developed and partly destroyed by the adherence to sac wall; and there is evidence to show that they have never been closed but represent a persistent neural groove which has been overgrown by adhesions and integument.

In Case IV this is capable of direct proof, as is shown in fig. 14, Section C, where partly differentiated epithelium of mixed neural and integumentary character is found on its external surface. In Cases III and V the overgrowth of skin epithelium has obscured the defect to a greater extent, but the lateral spreading of the nervous tissue, the absence of central canal and the position of nerve-roots with reference to the ribbon-like band of cord tissue, indicate that in these cases also the initial lesion has been a failure of closure of the lower sacral segments. Later, the meningeal layers have grown over the defective area, and to a less marked extent over the open medullary ribbon in Cases I and II; and still later the skin epithelium has covered the whole, and the adhesions mentioned have destroyed any vestiges of

ependymal cells which may have been present. It has already been noted that in complete lesions involving the whole of the neural tube (Case II) there is a tendency for skin to grow over the lower part of the defective area; the tendency of the skin epithelium even in the adult body toward growth is clearly shown in all granulating superficial wounds.

The accumulation of fluid in the meningeal part of the sac is always in these cases a secondary occurrence, and accounts for the dragging of the normal cord outwards. The accumulation of fluid in the cord tissue itself is a result of its abnormal adhesion. No satisfactory explanation of the collection of fluid in either the meningeal or the medullary sacs has yet been given. It cannot be even suggested from a study of these cases alone, but involves the consideration of the whole subject of the normal production and absorption of cerebrospinal fluid and all the possible abnormalities thereof.

CASE VI.

Myelocoele rachischisis completa restricta of Class 3, A.

Specimen No. 802, University of Texas Pathological Museum.

The specimen is of a full-term white female, length 38.5 cm. from vertex to coccyx. The external appearance is normal except for a considerable degree of hydrocephalus and a lumbo-sacral spina bifida. The head had been lacerated to promote delivery, and there are forceps marks upon the thighs. The body is somewhat degenerated, but there is no evidence that death had occurred before the beginning of labour. The degeneration appears to be the result of imperfect preservation, as the body had evidently been allowed to dry, and then had been placed whole in fixing fluid without any injection. For this reason the examination is in some respects unsatisfactory.

Dissection.—The head measures 49 cm. in circumference, but there has been some collapse which cannot be accurately estimated. The brain has been entirely destroyed by stuffing the cranial cavity with cotton, so that only a small irregular mass of tissue remains at the base, which cannot be identified by the naked eye, and its preservation is such that microscopical sections are of no value. The exposure of the vertebræ from behind shows that all the cervical, all the thoracic, and the first three lumbar vertebræ are normal. The laminae of the fourth lumbar meet in the median line, where they are fused by a cartilaginous union, but they do not possess any spinous processes. The laminae of the fifth lumbar are directed towards the median line, but are separated from each other by a space of 7 mm., which is bridged by a band of connective tissue. The sacral laminae flare outward, and are somewhat smaller than normal. The coccyx appears to be normal.

These lower vertebræ from the fifth lumbar to the last sacral are covered

externally by the parchment skin of the myelocele, of which the external appearance is shown in fig. 20, B. It will be described in detail later.

Dissection of the spinal cord and meninges above the level of the fifth lumbar vertebra shows that the meningeal layers are normal, but the dural sheath is somewhat collapsed, the epidural space being occupied by a gelatinous exudate, and the vascular and fatty tissue normally found here is reduced in quantity. The spinal ganglia are normal in size and position in all this region of the cord, but the dural sheaths of the spinal nerve roots, which should incline very slightly caudalward in the lower thoracic and lumbar areas, have a transverse direction. On opening the dura-arachnoid the cord is found to be soft and poorly preserved, so that only with great care in handling can

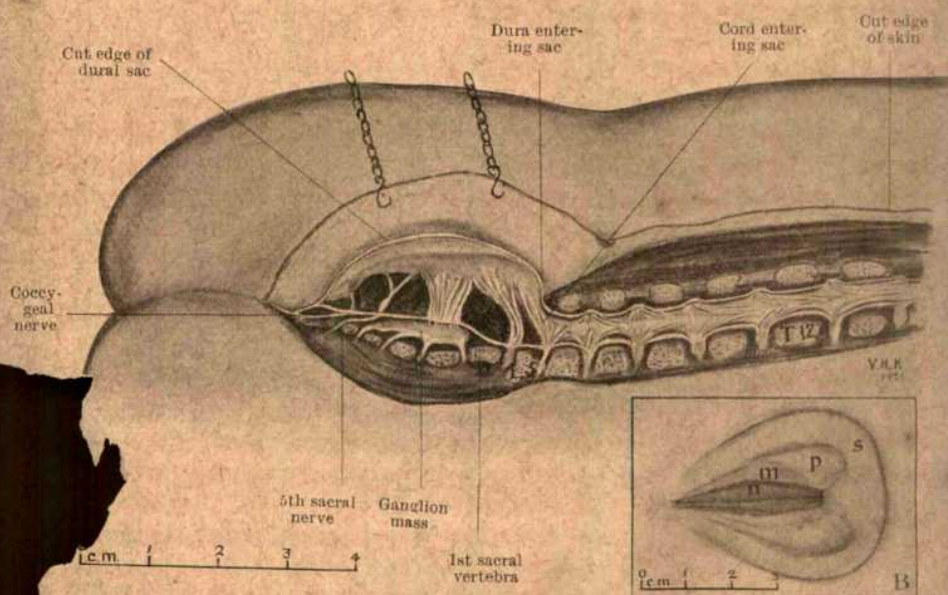


FIG. 20.—Case VI, lumbo-sacral myelocele. Dis-section of right side of myelocele. B, external appearance.

The nerve roots be traced. Those roots from the cervical and upper ten thoracic segments are normal in direction (cf. fig. 5, B), the tenth thoracic roots arising from the cord at the level of the body of the ninth thoracic vertebra. From this point they tend to lose their downward inclination, and present the relationships shown in fig. 20, A, that is, the ninth thoracic roots arise from the cord at the level of the tenth thoracic vertebra; the twelfth thoracic roots from that at the level of the eleventh thoracic vertebra; the first lumbar roots from the cord at the level of the second lumbar vertebra; the second lumbar from the cord at the level of the third lumbar vertebra; the third lumbar roots from the cord at the level of the fourth lumbar vertebra. The fourth and fifth will be found to have the same relation of the

myelocele. The condition of the cord is not such that any further examination can be made; it appears to be considerably smaller than normal, but definite evidence of collapse of a cystic condition remained.

Myelocele.—The parchment skin of the myelocele is somewhat wrinkled but flat, and there is no sign of a previous distension with fluid. It measures 35 mm. in transverse and 45 mm. in vertical diameter, and extends from the level of the fifth lumbar vertebra to that of the fourth sacral. At the level of the fifth sacral in the median line the skin is normal; a small tuft of fine hair is present here, but this is no more than is frequently found in this region in normal infants. The character of the wall of the myelocele is of considerable interest. As is seen in the drawing (fig. 20, B), it is pyriform with the apex directed caudalward. The upper part is rather sharply marked off from the surrounding skin by a groove, which disappears in the lower third of the "pear." Within this for a distance of 12 mm. at the broad end, and 10 mm. at the narrow end of the sac, the skin (s) is normal in appearance, except that it is slightly elevated above the level of the surrounding skin. Within this there is an irregular zone of wrinkled parchment skin, delicate in texture, without fatty layer; under a hand lens it shows fine hair and pores. At the upper part of the sac this zone (p) is blended with a very narrow zone of membrane (m), without evidence of epithelial covering, i.e., a meningeal layer; but at the lower part there is no such zone. Down the mid-line of the sac lies a band of brown tissue (n) which has the appearance of being covered by dried blood. This merges above and below into the skin surface of the peripheral zone of the sac, but laterally it is fused with the meningeal zone. The specimen had become dry before it was placed in preserving fluid, for the band of tissue, which is obviously the medullary groove, is contracted hard, but there is no degeneration of this region which interferes with dissection of the lesion.

Dissection (fig. 20).—The myelocele was surrounded by a circular incision and the skin surrounding it dissected up with its subcutaneous layer turned towards the median line. At the inner margin of the peripheral zone of the skin (fig. 20, B) the subcutaneous fatty layer disappears and a meningeal sac is found. The limits of this correspond very closely with the outer border of the flaring sacral laminae, but caudally it extends no lower than the fourth sacral vertebra. On cutting through the lateral margin of this and reflecting it, the dorsal wall of the sac is found to be composed of a fusion of dura and arachnoid with surface epithelium, and to pass medially into the medullary ribbon. The ventral wall is composed of dura and arachnoid and lies in contact with the exposed dorsal surfaces of the flaring laminae of the sacral vertebrae. In order to study the relationships of the medullary ribbon more fully, a bridge of connective tissue arching over the gap between the fifth lumbar and first sacral laminae was dissected away and the pedicle of this was cut. The foramen for the fifth lumbar nerve was also removed. The flaring laminae of the sacrum were also removed, exposing the posterior surface of the medullary ribbon.

At the level of the fifth lumbar vertebra the dural layer of the sac passes under the fibrous arch into the spinal canal. The opening in the dura was continued from the sac below to that already made in the sheath of the cord above, exposing the spinal cord as it passes from the canal into the upper part of the sac roof, where it becomes continuous with the medullary ribbon. In fig. 20 this dissection is shown on the right side. It will be seen in the drawing that the traction of the reflected area of the sac has pulled the cord and medullary ribbon out of the vertebral groove in which they lay, and the length of the closed part of the cord, from the neck of the sac to the roof, is somewhat exaggerated. The fourth lumbar nerve roots arise partly from the cord in relation to the fourth lumbar vertebra (above the sac) and partly from the closed cord as it passes under the fifth lumbar fibrous arch to the medullary ribbon. The fifth lumbar root arises from the proximal part of the medullary ribbon; its ganglion is normally situated. The roots of the upper four sacral nerves of the right side are grouped together so closely that no absolute differentiation between individual nerves, nor between anterior and posterior roots can be determined. This clump of fibres passes through the dural floor of the myelocoele, and into an elongated mass of nervous tissue enclosed in a prolongation of the dural sheath, lying in the groove representing the open sacral canal. From this, nerves can be traced to the upper four posterior sacral foramina. It therefore represents the upper four sacral ganglia fused into one mass. Certain of the proximal radicles of this clump appear to pass medial to the ganglionic mass and directly into the anterior foramina, but the tissues are so delicate that this cannot be definitely proved without more destruction of the specimen than seems justifiable. From the medullary ribbon distal to the clump of roots described, two delicate roots, on one of which there is a small ganglionic mass lying *within* the dura, pass out as the fifth sacral nerve. Still more distally a delicate strand passes down from the ribbon; this probably represents the coccygeal nerve, though it is too delicate to be definitely identified, and no ganglion could be found upon it. Distal to this the medullary ribbon, which has narrowed to a sharp point, passes into a slender fibrous strand and by this is connected with the dural floor of the myelocoele, and through this to the coccyx and subcutaneous tissue over it.

On the left side the connective tissue is similar except that the first sacral root has a normal ganglion, and the condition is a posterior radicles can be differentiated. The ganglia of the second, third and fourth sacral are grouped into one mass, on the right side. The fifth, third and fourth sacral has a well-developed ganglion occupying its normal position outside the fifth sacral sheath of dura. It should be mentioned that there is some doubt as to the spinal ganglionic character of the intradural mass on the right fifth sacral root as to the ganglion is smaller than normal, and indeed the roots on this side are much smaller than the corresponding roots on the left side. The root very close to the medullary ribbon is much smaller than the other. There was no other ganglion on this root; for various reasons no section of this minute body was made.

Microscopical examination.—An attempt to procure material for examination

of the cord above the lesion was an absolute failure. The tissue was so degenerated that nothing could be done with it. The tissue of the myelocoele was hard but well preserved, as was the ganglionic mass. The sections were taken from the fifth lumbar and first sacral segments (fig. 20). It seemed best not to destroy the specimen for museum purposes and therefore no serial sections were made below this level.

Section 4 (fig. 21, A).—Just below the attachment of the cord to the roof of the myelocoele, representing the level of the first sacral segment of the cord. On the right side the skin surface shows many sweat glands and numerous small hair follicles which are more deeply situated than normally. This zone of skin is that marked "n" in fig. 20, B. It passes rather suddenly into a fibrous layer "m," apparently meningeal, but covered by a thin layer of stratified squamous epithelium which has no papillae nor other integumentary structures. This zone in turn passes medially and the fibrous layers are fused with the pia which lies ventral to the ribbon cord. The layer of surface epithelium ends rather abruptly on this side of the specimen in a mass of epithelial and blood cells which separates it from the outlying (posterior) portion of the ribbon cord. One small mass of glia is found in the fibrous tissue just lateral to this hæmorrhagic area, and is covered by the surface epithelial layer. On the opposite (left) side the relations are somewhat different. The surface epithelium passes medially over the outlying area of ribbon cord and there terminates abruptly, and lateral glial masses of considerable size are found beneath the epidermis, separated from it by a thin layer of fibrous tissue which apparently represents corium. Non-myelinated posterior nerve-roots approach the glial masses on each side; on the right they are situated just beneath the hæmorrhagic zone; on the left, they appear to enter the cord where the surface epithelium terminates.

The structure of the medullary ribbon does not differ materially from that of the ribbon cord in Case I. Anterior horn cells are well developed; anterior nerve-roots are present but are not myelinated. At the middle line there is a depression corresponding with the central canal, and beneath it a narrow anterior commissure. This depression and the surface of the ribbon cord contiguous to it are covered by ependymal cells. The anterior white matter lies median to the spreading anterior grey horns. This region of the medullary ribbon is oedematous, and there are great numbers of small blood-vessels coursing through it. The majority of these are in the form of definite trabeculae of connective tissue. Laterally there remain these are in evidence of the posterior portion of the cord, except the glial mass but little is noted as lying lateral and separated from the main medullary masses already noted as lying lateral and separated from the main ribbon apparatus. The small posterior portion is not separated from the main ribbon apparatus. The tissue is made up of glia and possibly nerve-fibres without any evidence of ears to be made of cells. There are myelinated fibres anywhere in the section.

The sections 2 mm. caudal to this show no great change except a gradual decrease in the number of anterior horn cells and the increase in the vascular invasion of the cord structure. The isolated glial masses noted

CASE VII.

Meningocele—rachischisis incompleta restricta of Class 1, B.

History.—D. M., female, aged 11 months, John Sealy Hospital.

No family history of deformity nor nervous lesion. Child is healthy and well-developed except for the presence of a lumbo-sacral tumour. Control of bladder and bowels appears to be normal. Baby presents a small congenital tumour covered by parchment skin, about $1\frac{1}{2}$ in. in diameter, occupying the sacral region. It is tense, its surface is unbroken, and is slightly painful on

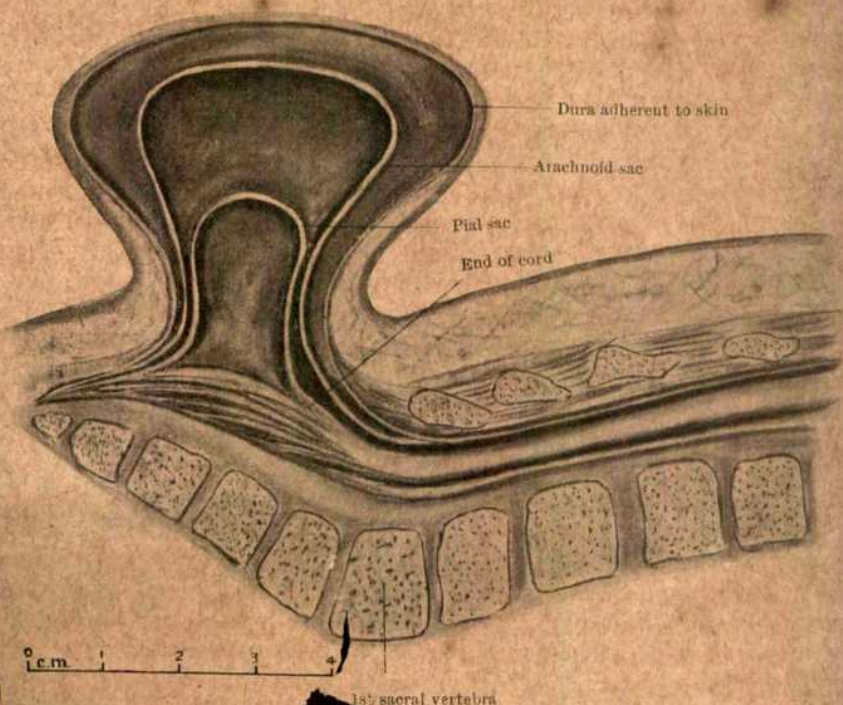


FIG. 22.—Case VII, meningocele. Anterior surface of cord shown as seen at operation. No dissection regarding nerve roots.

pressure. Operation,
anesthesia. Transverse

Thompson, September 18, 1918, ether

It was opened and its walls sutured over the *cord* (not *cauda equina* alone) which was found to lie inside it; the portion of cord lying in its proximal portion was not disturbed. The second sac, which was thought to be dural, was partly dissected away, and its edges sutured; and the parchment skin of the external sac was removed until normal skin was reached and this was finally sutured. Convalescence was ideal, and the baby was dismissed from the hospital, September 26. Later history: February, 1921, the mother reports that the child's general health is good and that she is bright mentally. She began to walk at the age of 18 months; at first she had a tendency to "turn the feet in," but this is improving. She has very good control of the bladder, but not of the bowels.

Discussion of case.—Unfortunately this case occurred before the writer's interest in spina bifida had been awakened, and the small portions of the meningeal sacs which had been dissected away in the operation were not preserved. The diagram shown in fig. 22 is reconstructed from a drawing of the sac layers made at the time of the operation. In the light of the conditions in other cases it is probable that the sac thought at operation to be dural was a thickened arachnoid sac, and that the inner sac was composed of the outer layer of the pia. The outer parchment skin was lined by a glistening membrane and filled with clear fluid, and this doubtless represented the fused integument and dura, as in other specimens described. The thickening of the arachnoid of the inner sac, which led to the misconception at the time of operation, is entirely in accordance with observations on Case IV, in which a partial transverse septum of arachnoid is found. The position of cord tissue in relation to the upper part of the innermost sac clearly indicates that this is pia. The drawing has been labelled according to this interpretation in preference to that made at the time of operation.

The feature of peculiar interest in this case is the presence of cord tissue in the floor of the upper part of this sac. The nervous tissue observed was spinal medulla and not the nerve roots of the cauda equina. It is obvious that no detailed examination of this nor of the cauda equina could be made. This much, however, was discovered, that the cord extended as far as the floor of the meningocele, i.e., as low down as the fifth lumbar vertebra, though it should end at the second. This indicates that in this case, in which apparently no structures except the meninges (and skin) were involved, there was at some time in the development additional derm sufficient to bind the neural tube down in the vertebral canal. This is a feature of many of the cases of spina bifida which have been studied. It is of considerable consideration in the study of the development of the nervous system.

For this reason all statistical and practical considerations have been deferred to this place. Neither time nor opportunity has sufficed for a complete study of all the available writings on the subject, yet it is hoped that this survey, in spite of its incompleteness, will not be without value. All matters which do not have a direct bearing on the anatomical study presented have been omitted.

Statistical Summary.

Frequency.—The Report of the Committee on Spina Bifida of the London Clinical Society, presented to the Society in 1885, cites the following frequency statistics: "Dr. Demme found 57 cases of spina bifida in 36,148 children; Chaussier records 22 cases among 22,293 children in the Paris Maternité." Harrar, in 1916, found 59 cases of spina bifida in 91,600 births in the Lying-in Hospital in New York. Grouping these figures we have an incidence of 1 in 900 births. Joseph gives the frequency of "spina bifida with tumour" as 1 in 1,000 births. Both these percentages omit the cases of spina bifida occulta, since these are not discoverable in the infant except in very rare cases. S. N. Clark gives the percentage of spina bifida occulta as 5 per cent. of all cases, but he evidently refers to cases giving rise to nervous symptoms. The mild varieties in which cleft of the laminae or of the spines alone occurs without symptoms of pressure on the cord are fairly frequently encountered in the dissecting room. No facts regarding the percentage of all cases which are sufficiently limited to be of surgical importance are available.

Locality.—In 385 operative cases treated by excision, collected by J. E. Moore in 1905, the locality is given as follows: 23 per cent. sacral; 34 per cent. lumbar; 24 per cent. lumbo-sacral; $4\frac{1}{2}$ per cent. thoracic; $9\frac{1}{2}$ per cent. cervical; two cases were occipital. This represents the localization of the restricted (operable) variety of lesion only, but it is in such cases that locality is of practical importance.

Type of restricted lesions.—Unfortunately Moore does not give the percentages of different types of tumour encountered in his collection; doubtless in many of the cases he collected there was no specific information regarding this feature. Fenner places meningoceles at 10 per cent. and meningo-myeloceles at 70 per cent. to 80 per cent. of the cases. In a total of 170 cases in which accurate anatomical data are given, collected by the writer from the literature cited in the bibliography appended to this paper, the percentage is as follows: 7 cases ($4\frac{1}{2}$ per cent.) spina bifida occulta (with symptoms); 4 cases (2·3 per cent.)

"meningoceles with adherent cauda equina"; 36 cases (21.1 per cent.) pure meningoceles; 120 cases (70.6 per cent.) myelo-meningoceles; and 3 cases (1.7 per cent.) syringo-myelo-meningoceles. As the meningoceles only in this series presented no nervous lesion, this indicates that 78 per cent. of all restricted cases involve the cord or its nerve-roots to some extent. From the point of view of operability and functional result this is a matter of prime importance.

Complications.—In non-viable cases unassociated anomalies—hare-lip, ectopia vesicæ, non-paralytic club-foot and other more widespread abnormalities—are very common. In viable cases they are less frequent, but still sufficiently so to call for comment.

Nervous complications are of even greater frequency. Among 359 cases collected by the London Clinical Society, in which the complications are stated, 46 had hydrocephalus. These are cases in which the patients had restricted lesions. Harrar in the records of 68 cases in the Lying-in Hospital found 23 cases of primary hydrocephalus and 10 developing hydrocephalus following operation. The greater number which he found are doubtless due to the fact that his records include all cases observed, whether viable or not.

No facts regarding the incidence of hydromyelia are available. From my own very limited experience it appears to occur in a high percentage of those cases in which the cord is involved in the lesion, whether there be hydrocephalus or not. Thus in Cases I and VI there was hydrocephalus and hydromyelia above the open cord segments; in Cases III, IV and V there was hydromyelia without hydrocephalus. Information regarding the condition of the cord in the single case of meningocele reported (Case VII) is necessarily lacking. The small proportion of restricted cases which show sufficient dilatation of the cord to fall into the class of syringo- (or hydro-) myelo-meningocele, represents, therefore, only an exaggeration of a fairly frequent condition. Further investigation along this line is urgently needed. Post-mortem examination is not always essential to this, since careful examination of the cut end of the cord at the time of operation on cases with attached cord will reveal any considerable dilatation which may be present, and while the extent of this lesion upward may remain uncertain, it appears to be practically certain that a dilatation which is plainly visible at this point involves a considerable number of segments above. All cases in which complete autopsy findings can be obtained should be investigated with reference to this feature.

Paralyses of the sphincters or of the legs, and loss of sensation

over areas supplied by nerves involved in the lesion, are encountered in the exact proportion in which one finds involvement of the cord in the lesion, and are a direct result rather than a complication of the disease.

Course of the disease.—A large proportion of untreated cases die within a few months. Thus of 649 deaths due to spina bifida, occurring in England in the year 1882, most of them in untreated patients, 612 were in the first year of life. Of 68 cases reviewed by Harrar (59 born in the Lying-in Hospital and 9 others sent in for operation) 7 were stillborn, and 29 died untreated within a few weeks. The other cases of his series were submitted to operation. Of 49 fatal cases of untreated restricted lesion collected by the writer, in which the cause of death is definitely stated, 14 died of marasmus, 7 of intercurrent infection, 2 of hydrocephalus, 23 of rupture of the sac, 3 of convulsions (i.e., meningitis). Accurate statistics of such untreated cases are very hard to obtain since untreated cases are but rarely recorded. In but a very small proportion even of the mild defects is there hope of recovery without operative interference, yet in a few of the less severe cases spontaneous cure occurs. In the 60 untreated cases recorded by the London Clinical Society, 14 cases (23·3 per cent.) were cured in the following manner: in eight there was a gradual shrinkage of the sac; in one it ulcerated and oozed for some time; in four it burst and later shrank away. The shrinkage of small tumours in this way probably accounts for a certain number of cases of spina bifida occulta, while others may be accounted for by a similar reduction of the tumour in intra-uterine life.

Operative mortality.—In Moore's series there was 27 per cent primary mortality, with an additional 7 per cent. within three months after operation, bringing the total to 34 per cent. When one considers that the cases which are operated upon are all selected cases, this primary mortality is exceedingly high; moreover, a secondary mortality is to be expected, apart from operative interference. Moore considers that "if all cases had been followed and reported, the probability is that the mortality at the time of, and a few months subsequent to, operation would be fully 50 per cent." In view of this he considers that operative interference in children under 5 years of age is scarcely worth while, since it appears neither to reduce the natural death-rate nor to be attended by great functional success. On the other hand he takes the position that children who have survived to that age may be submitted to the risk of operation.

As opposed to this view there is the great danger already alluded to, of rupture and ulceration of the sac. In 117 untreated cases collected from the appended bibliography, rupture of the sac occurred 27 times. In 97 of these cases in which the character of the sac is recorded, there was ulceration in 24. In the five restricted cases considered in this report, there was rupture in one, gross ulceration of the sac in two, and microscopical evidence of inflammation in the shape of polynuclear and round cell infiltration in four. One sac was not examined microscopically. In the case in which Morton's fluid was used death occurred immediately upon the injection, so that the inflammatory exudate was present prior to this treatment. Harmer found ulceration in 64.7 per cent. of his 34 cases. He further points out that he has found rupture of the sac in patients a few hours old, and suggests very early operation because of this danger and that of ulceration with subsequent meningitis. In view of the fact that few untreated cases are recorded it seems probable that these complications occur even more frequently than the figures would lead one to suspect. The primary operative mortality, so largely due to infection, might be materially decreased by very early operation, even though the secondary mortality, which depends mainly upon hydrocephalus and marasmus, be correspondingly increased. There appears to be no reason to consider that operation increases the percentage of hydrocephalus, in view of the large percentage occurring without interference and the number of cases that are accompanied by hydromyelia. It must be borne in mind in considering this that the majority of successfully operated cases (i.e., those which do not succumb to the immediate effects of operation, as shock, infection, &c.) live longer than do untreated cases, and therefore a higher percentage die of hydrocephalus which would otherwise have died of the meningocele itself (rupture, meningitis, &c.). Many surgeons, however, recognizing the high incidence of hydrocephalus, prefer to wait some months for its development before undertaking an operation which they feel may be useless.

Theoretical Considerations regarding Surgical Procedure.

Operability.—The question of operation upon cases with associated hydrocephalus, paralyses, &c., must remain largely a matter of individual opinion. It is purely from the point of view of the anatomical facts that I propose to discuss it. There can be no doubt that pure meningoceles should be operated upon, and in view of the possibility of

ulceration or rupture of the sac they should be treated early. Moreover, shock is almost certainly less in operations upon the spinal cord of young infants than in older children. Spontaneous cure is not to be expected in the great majority of cases, and the risks run by awaiting it are too great. In the cases in which there is some doubt as to the presence of nerve elements in the sac, evidences of paralyses, especially of sphincters, and anæsthesia round the anal margin or on the back of the thighs, are of value. Ulceration of the sac wall, a thickened band down the middle of a thin sac wall, and a vascular granulating surface with umbilication, are valuable diagnostic indications of adherence of the cord. The presence of skin covering the whole of the sac does not rule out myelocoele. It must be borne in mind that meningoceles are infrequent and myelomeningoceles frequent, but that but few meningoceles have broad bases. Transillumination of the sac has been suggested for finding the presence of nerve roots, but it seems possible that this might lead to error, as adventitious meningeal adhesions sometimes occur. In contemplating operation on those cases in which cord is known or suspected to be present, one should consider that in this type spontaneous cure is practically never attained; that ulceration is exceedingly frequent and meningitis therefore the almost inevitable outcome; that not only is the cord below its attachment to the sac practically useless, but the attachment is dragging upon the relatively normal cord above and jeopardizing its function. This is a matter which has not been given due weight in considering the advisability of operating in this type of case, though the traction on the cord has been recognized by all careful investigators, as is shown in the diagrams of my cases. Damage already done cannot be repaired by relief of tension, but at least the conditions can be rendered more nearly normal for the further development which goes on after birth.

Methods of treating the sac.—Stress has always been laid upon the careful dissection of nerve roots from the sac wall, and rightly so, if they can be attached to a relatively normal cord. Many observers, however, have recognized that the nerves were inseparably bound to the wall of the sac and have failed to realize the true significance of this. They have not seen in the thickened band of sac roof, to which nerve roots are attached, the malformed, practically useless segments of the cord without which the nerve radicles are valueless, and have dissected free roots that serve no purpose. La Ferte and others, recognizing the importance of preserving the cord, have attempted to turn in the portion of the sac in which it is attached, with the result that meningitis has



followed with great frequency. When one considers that it is almost impossible to dissect free any of this attached part of cord, and that inevitably one must leave some skin with it if one preserves all the nervous elements, the avoidance of meningitis becomes practically impossible. Nor does it appear to be wise to make this attempt in view of other matters. The cord segments distal to the point of attachment to the sac roof, as shown in this report and in other similar cases reported by previous investigators, are so poorly developed and so damaged by inflammation and epidermal overgrowth, that they are practically functionless; this can be demonstrated histologically and by the neurological examination of the regions normally supplied by them. There is, therefore, nothing to be gained by their preservation. All that can be hoped for is that the segments above the cord lesion may be so far as possible preserved from further harm. To accomplish this the end of the cord must be cut free and allowed to slip up into the canal.

An adherent plug of sac wall left by the operator is comparable anatomically to the adhesion of skin or fibrous tissue to the cord found in spina bifida occulta. Theoretically at least delayed traction or pressure symptoms may be expected here as in the primarily occult cases. Nor can one overlook the danger of an inclusion dermoid developing from the buried epithelial cells of the sac wall. This is especially the case where skin covers or almost covers the whole of the roof of the sac, for in such cases deep skin glands may lie in almost direct contact with the lateral parts of the cord tissue. These delayed effects are not ordinarily reported, because but few cases where the patient survives to adolescence report to the surgeon who has operated, and this is probably particularly true of the cases with no symptoms. Such patients, dissatisfied with the result of the first treatment, are likely to seek some other surgeon who is ignorant of the precise anatomical state and method of procedure at the primary operation. It is difficult to trace successful cases after a number of years have elapsed; it is even more difficult to trace failures. In the case of the anatomical condition in cases with attached cord, therefore, the rational procedure is to cut free the cord as close to sac wall as possible without leaving any attached inflammatory or surface epithelium, and to injure as little as possible by ligature or by handling the ends of this normal cord and the nerve roots attached to it. From purely theoretical reasons it would appear to be preferable to ligature the anterior median vessels with very fine ligatures without including the entire cord, since compression of the cord within the pia

a considerable portion of it. Exceedingly delicate ligatures and a very fine needle should be used for this, and the ligatures used as tractors to steady the cord while it was being freed from the sac wall. With a view to preserving as much as possible of the healthy cord the line of section should be made parallel with the sac roof and not transversely across the cord. It should also be directed to the nerve radicles which arise from the lower portion of the cord. Nerve roots in connection with the lower segments within the sac run in contact with the roof of the sac. To this they are adherent, and finally they pass back freely through the sac to their foramina. This fact is demonstrated in Cases III, IV and V. The difficulty in recognizing them is caused by their abnormal direction and adherence to the sac, so that they appear to arise from the involved segments of the cord in the sac wall. If the intra-cystic portion of the cord is carefully examined these roots may be traced from their origin and should then be carefully freed from the sac wall before the cord is cut free. If the anatomical relations are kept clearly in mind the recognition and dissection of these roots should not be impossible under the conditions of operation. The increase in paralysis after operation, often encountered in this type of case, is probably in many instances due to section of these radicles, and not to the section of radicles which arise from the segments of cord which are adherent to the sac wall.

Post-operative recovery.—Except in the cases of spina bifida occulta with pressure symptoms, and in a small number of meningoceles in which there is adherence or traction of the nerve roots but no lesion of the cord, no improvement in function is to be expected as the result of operation. What may be hoped for is that the function of segments above the lesion will not be subjected to further impairment by the presence of fluid or the presence of inflammation. In but few cases even of pure meningocele is there perfect function of the sphincters. This leads one to suspect some cord involvement, perhaps only to the extent that the closed cord is drawn down out of its normal level into the floor of the sac. This probably indicates, as noted in the description of Case VII, that the initial lesion was in the neural ectoderm and that the development of the lower segments of the cord was interfered with to some extent. In operating upon these cases, therefore, one must be prepared for some loss of function of the sphincters, and must remember the difficulty of determining this accurately in the very young child. It appears to be practically impossible in many cases to

determine without undue risk to the patient whether the nervous tissue lying in the floor of the sac is the caudal-equina, as it should be in a lumbo-sacral tumour, or the end of the cord itself. Nevertheless, this should be determined as nearly as possible, and where there is any doubt in the matter this doubt should be stated definitely in the notes. After reading many case reports in which cord and nerve radicles were said to be absent from the sac, and yet there was incontinence of urine and faeces either before or after operation, one cannot help feeling that some uncertainty existed at the time the observations were made. This is a matter of considerable importance for the surgeon, since the operation which is followed by incontinence where none has been predicted is distressing, and leads the parents to blame the operator though he may not be at fault.

Where there is paralysis of the legs, it may be taken to indicate almost certainly that there is an adherent cord in the sac, and in view of its poorly developed and degenerated condition it may be further assumed that the paralysis is not remediable, even in the rare cases in which circumstances will permit the preservation of part of the degenerated cord. For the purpose of prognosis and also for the advancement of the general scientific knowledge of the subject, the sac wall in such cases should be submitted to systematic microscopic examination. Until this is done and careful reports of the state given with case reports, the results of different methods of treating the sac, and especially the prognosis of different types of case as regards late functional results, cannot be raised above the level of speculation. In this connection it may not be out of place to recall the statistics of Saatchleben (quoted from Harrar), who found in an analysis of thirty cases from the Mikulicz clinic that five only were permanently cured, and these were meningoceles. Harmer in his thirty cases found some paralysis in twenty. This was increased after operation in three; not affected in nine; and improved in eight. Of these eight, five were slightly improved but died subsequently of hydrocephalus or infection. One with pre-operative incontinence showed improvement fifteen months later; one with paralysis of the foot and loss of sensation in both legs recovered from the paralysis; one showed no change in the sensory loss; one with paralysis of the legs was well sixteen months later. From this evidence, Harmer concludes that paralysis is in some cases due to traction: a strong argument in favour of operation on cases with attached cord.

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OBSERVATIONS ON CEREBELLAR STIMULATIONS.

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THE question whether the cerebellar cortex is capable of responding to electrical and other forms of stimulation is at present unsettled.

André-Thomas [1], who gives a résumé of the earlier literature, notes that stimulations evoke less constant effects than experimental destructions. He also comments on the great diversity of opinion expressed: some observers attribute definite responses to the various regions stimulated; others deny the excitability of the cortex, whilst admitting it for the intracerebellar nuclei.

The view last expressed is that maintained by Horsley and Clarke [7], who ascribe the results occasionally yielded by cortical stimulation to spread of current to the intracerebellar nuclei. They emphasize a fallacy, which doubtless entered into much earlier work, namely, facility with which the effects of excitation may be vitiated by current escape to the nucleus and rootlets of the accessorius nerve.

As the outcome of researches on the dog and monkey, Rothmann [9] arrived at conclusions which diverge materially from those of Horsley and Clarke. Stimulating with the bipolar method, the animal being in morphine-ether narcosis, he found the threshold much higher than that of the cerebral cortex. Whilst admitting that some movements of the fore-limb may be due to current diffusion to the intracerebellar nuclei (dentate nucleus), he considers that certain characteristic t

movements in the fore-leg, elicitable from the anterior surface of the cerebellum, are an expression of genuine cortical excitation. He was able to prove that the impulses concerned in this response are conveyed by the superior peduncles and rubrospinal tracts.

It should be remarked in passing that the conclusions of this writer show but little agreement with the localization theory of Van Rynberk [10]; this theory has more recently been accorded the support of André-Thomas and Durupt [2].

Although Rothmann fails to comment on the mode of causation of the "running movements" ("Laufbewegungen") at times elicitable from the anterior part of the vermis, it is probable that he considers them due to excitation of the cortex. It may be inferred, then, that he regards the cerebellar cortex as excitable.

Beck and Bikeles [3], who repeated earlier experiments of Magnini, conclude that strychnine and phenol are without action on the cortex cerebelli, and, therefore, assert that it is inexcitable.

Shimazono [13], however, applied strychnine to the cerebellar cortex of the pigeon and observed an increase of muscle tonus on the same side of the body.

Beck and Bikeles [4], reverting to the problem, deny any increase of tonus in either pigeon or dog as a result of the action of strychnine on the cortex and, in consequence, reaffirm their original thesis that the cortex is inexcitable.

After denying the excitability of the cortex, the same authors assert, with curious inconsistency, in a subsequent paper [5], that cooling does not depress the *excitability* of the cortex. Failure to mention any definite reactions makes it appear probable that, whatever responses may have been induced, they were excited by action of the current elsewhere than on the cortex (trigeminal, accessorius or nucleus gracilis cuneatus, *vide* Horsley and Clarke [7]). Such an interpretation would afford a plausible explanation of the lack of change on cooling.

Similar criticisms apply to the conclusions of Bikeles and Myszkowski [6] that cocaine does not lower the excitability of the cortex.

Consideration of the conflicting statements outlined above reveals the desirability of further evidence regarding the question of the excitability of the cortex cerebelli. The idea that the cortical neurones are excitable appears natural and logical, and its proof demands only the evocation of a suitable test reaction, which might be evoked by currents of low intensity, the action of which would extend but a slight distance from the surface.

A reaction fulfilling these conditions was described by Sherrington [11]: when the anterior surface of the cerebellum is faradized there ensues an immediate inhibition of the "decerebrate rigidity" previously evoked by ablation of the cerebral hemispheres. Accordingly, this inhibitory response was employed in the present research as a means of deciding the question whether the cerebellar cortex is excitable.

In the course of this work faradization was applied to the superior cerebellar peduncle in a few instances. The only previous observations on this subject which have come to our notice are those of Thiele [14]. As a result of such stimulation he observed, in particular, movements of the ipsilateral fore-limb consisting of protrusion at the shoulder and flexion at the elbow.

METHODS.

The bipolar method of stimulation was chosen in the majority of experiments, since it appeared that the current would be confined to the cortical layers of neurones in a manner scarcely possible in the unipolar method. The platinum electrodes terminated in small beads 1 mm. apart. When precise localization was necessary recourse was had to the unipolar method, the stigmatic electrode being of the usual Sherrington type. The inductorium was operated by two storage batteries; an ammeter and rheostat were included in the primary circuit and the resistance was so arranged that, whilst the hammer was in vibration, the ammeter showed a reading of approximately 0.2 ampere. At 135 mm. secondary distance the current from the bipolar electrodes was just detectable on the tip of the tongue.

The animal (cat) was anaesthetized with chloroform and ether. Tracheotomy was performed and both carotids were ligated. Decerebration was performed with the decerebrator [12], the plane of the section lying about 27 mm. behind the frontoparietal suture, in a cat of medium size. The level of this section, somewhat anterior to that usually employed, was chosen on account of the necessity of preserving the tentorium cerebelli intact. The plane lies usually just in front of posterior colliculi. Following the decerebration a small serrefine, clamped on the divided basilar artery. The latter procedure permitted the immediate continuance of the experiment. The head was supported at a convenient height in a clamp applied either to the jaw or to the skull. Precautions were observed to keep the corneal condition by the application of swabs wet with warm solution.

RESULTS OBTAINED IN PRESENT INVESTIGATION.

When stimulation of appropriate strength is applied to the anterior surface of the vermis there results an immediate and general relaxation of the rigidity. The possibility that this inhibition is evoked, to any important degree, from the cut edges of the dura or through the trigeminus may be quickly excluded. The low intensity of the current (100 mm. sec.) and the position of the electrodes in the mid-line render it practically certain that no physical spread can occur to the dural margin or to the trigeminus, both of which are too far distant. Furthermore, we found that the application of 1 per cent. cocaine hydrochloride to the edge of the dura did not modify the reaction in any way. Hence, it may be concluded that the inhibition is evoked from the cerebellar substance.

Possible influence of the current on the internal nuclei in contributing to the effect must next be considered, and the evidence which renders this factor unessential will now receive attention.

In the first place a "healthy" vascular condition of the cortex is necessary for the production of the response by weak currents. The development of anæmia immediately abolishes the reaction. In these respects the cerebellar cortex closely resembles the cerebral cortex. Moreover, the inhibition is elicitable by weak currents (100 mm. sec.), which are, indeed, less intense than those required to excite the cerebral cortex; in one experiment the threshold for exciting hind limb movements from the cerebral motor area was not attained until the secondary coil was at 58 mm. This observation is contrary to those of Beck and Bikeles [5]; the possibility, however, has already been suggested that some, at least, of the reactions described by these writers were caused by current escape to the trigeminus or accessorius, rather than by direct stimulation of the cerebellar cortex. Under these circumstances the current strengths they employed would not indicate the degree of excitability of the cerebellar cortex. In support of such an interpretation of their results, we would mention that we observed that approximation of the electrodes to the vicinity of the trigeminus yields marked postural changes in the ipsilateral fore-leg, and that direct stimulation of the nerve itself with weak currents (100 mm. sec.) causes flexions and claw movements in the same limb.

The terms "vermis" and "lateral hemispheres" are retained in the present paper, since the nomenclature of Bolk and van Rynberk offers no advantages in relation to the problems investigated.

If we admit that the inhibition is called forth in the cortical neurones we may naturally expect abolition of the response by the application of cocaine. Accordingly, the response was induced from the anterior surface of the vermis by a minimal current and a 1 per cent. solution of cocaine hydrochloride containing a little methylene blue was then applied. Stimulation of the original intensity repeated after about one minute yielded no response. It is reasonable to suppose that the influence of the cocaine was mainly on the cortical neurones and that, therefore, the inhibition had been induced as a result of excitation of these neurones.

The evidence given above leads to the logical conclusion that the inhibition is induced as a consequence of a state of excitation in the cortical neurones or, in other words, that in respect to this reaction the cerebellar cortex is excitable.

Sherrington [11] describes the "inhibitory area" as extending over the anterior surfaces of the vermis and lateral hemispheres. With the intention of studying the cortical distribution of the response, we explored the cerebellar surface in other situations. In one experiment small portions of the vermis were successively exposed and each portion was tested with a weak current (98 mm. sec.). It was found that the vermis yielded inhibition from its most anterior part backwards to about 3 mm. above the medulla oblongata; farther than this it was impractical to go, owing to action of the current on the medullary centres. The inhibition affected all four legs; although the remainder of the body was not observed specially, it probably shared in the reaction.

Conclusions regarding the results of faradizing the anterior surface of the lateral hemisphere are only permissible when currents of low intensity are employed. In the case of stronger currents the possibility of diffusion to the cut dural margin or to the trigeminus or accessorius must be considered. Sherrington observed modifications of the rigidity as a result of stimulation of the edge of the dura. He also noted alterations induced reflexly through the trigeminus [11], whilst we ourselves (*vide supra*) obtained changes in limb posture as a result of the action of weak currents on this nerve. Our observations showed that the inhibition elicitable from the anterior surface of the lateral hemisphere reveals itself most intensely in the ipsilateral limbs and more noticeably in the hind-leg than in the fore-leg. Fig. 1 indicates the extent of the anterior cerebellar surface, on one side, from which the reaction was evoked.

The effects elicitable from the posterior surface of the lateral hemisphere have not yet been studied sufficiently to permit of drawing definite conclusions.

In a number of experiments faradization was applied to the superior cerebellar peduncle. In one experiment the cerebellum was removed; subsequently the rigidity first increased and then disappeared completely (cf. Weed [15]). Bipolar stimulation of the right superior peduncle (82 mm. sec.) then yielded rhythmical opening and closing of the claws of the right fore-leg together with running movements in both hind-

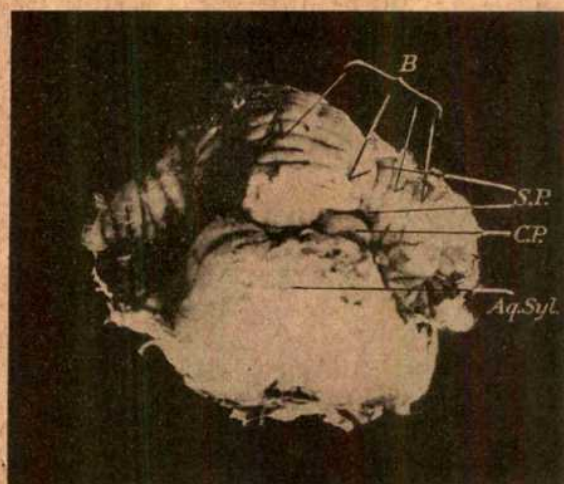


FIG. 1.—Anterior surface of cerebellum of cat. $\times 2$. Aq. Syl., aqueduct of Sylvius; B, bristles indicating extent of "inhibitory area" on one side; C.P., colliculus posterior; S.P., sulcus primarius (Bolk).

legs. The unipolar method was then substituted, the indifferent electrode being secured to the left hind-leg. Stimulation was applied to the same situation as in the bipolar method, the secondary being at 100 mm. There resulted the same type of claw movements in the right fore-leg; these movements are very characteristic and resemble those noted in a stroked cat. Because of the attachment of the indifferent electrode the hind-legs were not observed.

A bristle was inserted at the point yielding the reaction just depicted. Sections were prepared and were stained by the Weigert hæmatoxylin method. The bristle is found, on examination, to be situated in the right brachium conjunctivum (fig. 2). The electrode was applied at the point of entrance of the bristle into the brain-stem.

That the effects just mentioned are in reality due to stimulation of the brachium conjunctivum and are not caused reflexly is rendered practically certain, since claw movements of the same character were elicited by faradization of a point in the interior of the cerebellum at a particular stage in its removal. In this instance a tract destined to enter the brachium conjunctivum was doubtless stimulated.

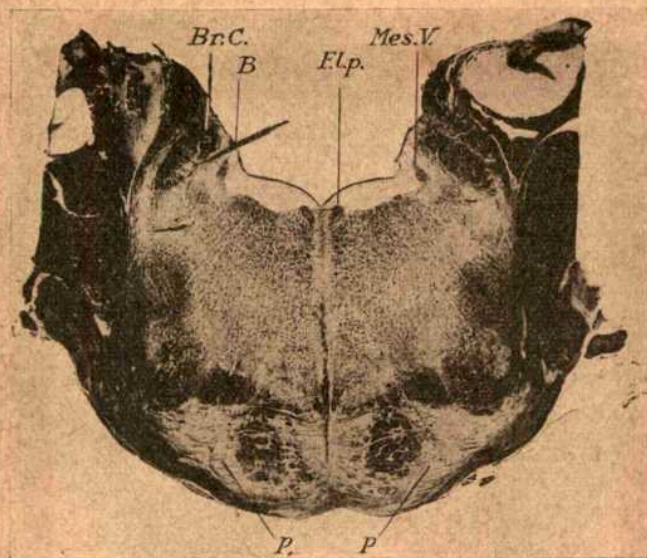


FIG. 2.—Section through the pons of a cat's brain. $\times 6$. *B*, point of entrance of bristle, indicating position of electrode by which claw movements were evoked in right fore-leg; *Br.C.*, brachium conjunctivum; *Fl.p.*, fasciculus longitudinalis posterior; *Mes.V.*, mesencephalic root of trigeminus; *P.*, pons.

We may conclude, therefore, that stimulation of the brachium conjunctivum induces claw movements in the ipsilateral fore-leg. With respect to the exact localization of the running movements of the hind-legs evoked by bipolar stimulation, further experiments are in progress.

Thiele [14], whose observations on stimulation of the superior peduncle were cited in the introduction, does not mention the occurrence of reactions like those noted in our experiments.

A variation from the usual inhibitory response of the cerebellum was noted in a few instances. Stimulation of the anterior surface of the vermis over the area outlined in fig. 3 resulted in the following sequence of events.

- (1) Inhibition of rigidity in both fore-legs;
- (2) Increased rigidity in the right fore-leg and inhibition of rigidity in the left fore-leg;
- (3) Walking movements of the fore-legs, during which the increase and decrease of tonus appeared reciprocally in the two legs.

Concurrently with these fore-leg reactions there developed in the hind-legs first walking and later running movements; movements of the claws also occurred in the hind-legs. The running movements recall the "Laufbewegungen" of Rothmann [9].

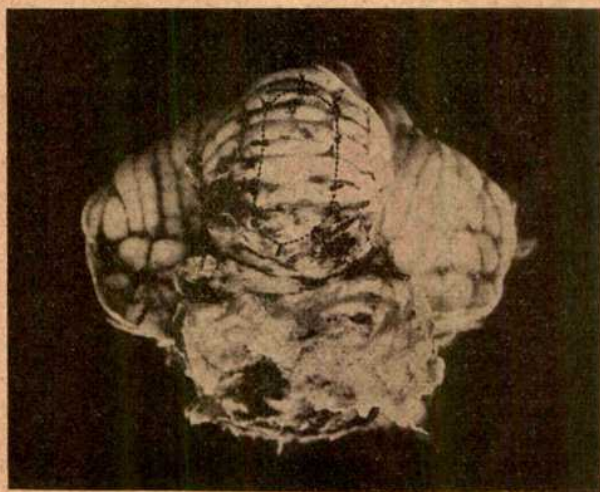


FIG. 3.—Anterior surface of cerebellum of cat. $\times 2$. Faradization of area enclosed by dotted lines yielded walking in fore-legs and walking and running in hind-legs. The figure shows the specimen after removal of part of the mid-brain subsequent to evoking the reactions described.

During the course of another experiment, in which stimulation of the same region yielded mainly inhibition of all fore-legs, it was once noted that a few walking movements of the hind legs resulted.

Since the walking and running movements just mentioned may be evoked with currents of low intensity which at times yield inhibition, and since the inhibition itself has been shown to be a cortical response, it is logical to conclude that the walking and running movements are also an indication of cortical activity. Hence these observations afford additional evidence in favour of our main thesis that the cerebellar cortex is excitable.

SUMMARY.

(1) Evidence is adduced to prove that the cerebellar cortex is excitable. The reaction chosen as a test was the inhibition of decerebrate rigidity evokable by stimulation of the surface of the cerebellum. Reasons are given for concluding that this reaction is induced as the result of a state of excitation in the cortical neurones of the cerebellum.

(2) The inhibition is yielded by the greater part of the vermis in an antero-posterior direction; it is also yielded by the anterior surfaces of the vermis and lateral hemispheres.

(3) Stimulation of the brachium conjunctivum causes claw movements in the ipsilateral fore-leg.

(4) Excitation of the anterior surface of the vermis occasionally elicits, as an alternative to inhibition, walking movements of the fore-legs and walking or running movements of the hind-legs. Since these reactions, like the inhibition, are induced by weak currents, they support our contention that the cerebellar cortex is excitable.

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THREE CASES OF SUPRA-PITUITARY TUMOUR PRESENTING FRÖHLICH'S SYNDROME.

BY CHARLES N. ARMSTRONG, M.B., D.P.H. DURH.

THE three cases about to be described are instances in which Fröhlich's syndrome was present in a more or less pronounced form associated with unusual types of tumour in the base of the brain, none of which started in or infiltrated the pituitary body. In the first two cases the tumour was a cystic ependymoma, and in the third case a cholesterin-containing cyst.

Case 1.—E. H., male, 10 years of age, was admitted to the National Hospital, Queen Square, under Dr. Gordon Holmes, on October 10, 1921, complaining of failing sight, headache and vomiting. His mother stated that the headaches and stiffness of the back of his neck began four months previously: the headaches occurred each afternoon, usually when he was returning home from school. Some weeks later he became subject to vomiting. After the summer holidays he returned to school on September 19, but remained there only a week: it was reported that he was not so bright as formerly and suffered from "heat-waves."

About September 29, after a restless night he complained of severe headaches: his pupils were dilated, he vomited about 10.30 p.m., and again a little later, and became drowsy.

His sight had been deteriorating since August and sometimes he complained of seeing double on looking straightforward. Three weeks before admission to hospital his mother noticed that his left eye squinted, turning inwards. This condition recurred once. During the last few months he had become much fatter.

No previous symptoms had been noticed, except that for the preceding two to three years he had complained of his hands being cold.

Examination.—A finely-featured well-nourished small boy 10 years of age, he looked younger than his years. Height 3 ft. 10 in.; weight 3 st. He was very drowsy and spoke in a somewhat tired manner with a hoarse voice. His skin was dry and exceptionally smooth and delicate. He was rather adipose generally with a feminine type of fat distribution over hips, abdomen, pubes and chest. The hands were small with long tapering fingers; his feet also were small and finely formed. The external genitalia seemed normal. No loss of sense of smell was detected. Visual acuity was much reduced

on admission; he could only see the largest letter on Snellen's Chart at bed length ($\frac{20}{60}$), vision being somewhat better in the right eye than in the left.

There was advanced papilloedema in both eyes, the swelling in the right reaching 3 D., and in the left 2 D.

The discs were becoming white and opaque-looking, and their vessels diminished in calibre.

Examination of the fields of vision was very difficult, as patient was very drowsy and difficult to arouse; they seemed reduced in the temporal halves and also to some extent in the nasal halves. The movements of his eyes were full. His pupils were dilated, circular and equal, reacting feebly to direct light and on accommodation. No abnormalities were detected in the function of the other cranial nerves, and the motor and sensory systems and the reflexes were unaffected.

His heart, lungs and alimentary system were normal. The systolic blood-pressure was 106 mm. Hg. Radiographic examination showed that the sella turcica was enlarged, chiefly in the antero-posterior plane. Unfortunately examination of the sugar tolerance could not be made as the administration of glucose caused vomiting.

On October 18, a right-sided parietal decompression operation was performed by Mr. Percy Sargent. About fourteen days later the patient was much improved; he was not so drowsy, had no pain and was brighter. His visual acuity increased to $\frac{20}{40}$.

As the ultimate prognosis seemed hopeless a second operation was undertaken for the removal of the tumour on November 2. The tumour was reached from the fronto-orbital route, the capsule opened and part of it removed by suction.

Post-operative notes.—The patient took small feeds quite well in the afternoon and the evening of the day of operation but did not regain full consciousness. The pulse was rapid and often difficult to feel. He collapsed and died in the early morning of the following day.

Pathological investigation.—A post-mortem examination was made on the same day. On removal of the brain a large tumour was found above the optic chiasma which it displaced downwards. After making a sagittal section through the brain, the tumour was seen to be in the mid-line; it was about the size of a walnut and was attached to the floor of the third ventricle throughout its whole length, and also to the infundibulum from the upper part of which it appeared to arise. The tumour was surrounded by a capsule except where it was united to the upper part of the infundibulum. It was semi-cystic and contained a highly-albuminous yellowish serum with numerous cholesterol crystals and some calcareous matter (fig. 1).

The sella turcica was greatly enlarged, evidently as a result of absorption of bone, while the posterior wall of the fossa had been pushed backwards by the tumour. The pituitary body itself appeared to be of normal size though flattened by pressure.

A section through the infundibulum and that part of the tumour adjacent

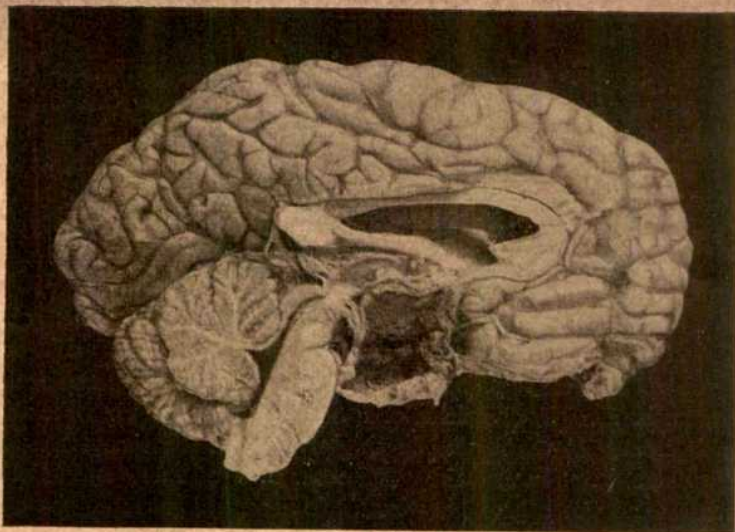


FIG. 1.—*Case 1.* Mesial sagittal section through brain, showing left half of tumour in position.



FIG. 2.—*Case 1.* Photomicrograph of section through the infundibulum and that part of the tumour adjacent to it, showing the proliferation of the cells of the ependymal lining of the recessus infundibuli. On the right side of the ependyma the normal neuroglial tissue of the infundibulum can be seen and on the other the cavity of the tumour containing organizing serum and calcareous deposits.

to it shows that the tumour is intimately connected with, and probably originated from, the ependyma of the infundibular recess (fig. 2). On the one side of the ependyma is the normal neuroglial tissue and on the other part of the cavity of the tumour containing organizing serum, some polymorphonuclear and mononuclear cells with pyknotic nuclei, and small areas of calcareous deposit. In the portion shown in fig. 2 the ependymal cells have proliferated and penetrated in both directions, but to a less extent into the glial tissue than into the tumour mass. Isolated clumps of these cells could be seen scattered through the infundibular tissue, while the tumour itself appears to be composed of strands of such cells enclosing spaces filled with serum and fibrin in which there are numerous calcareous deposits. These strands of epithelial tissue run in a matrix which is indistinguishable from glial tissue, and in this tissue run the blood-vessels which are numerous and have thin walls. The outer cells of these epithelial masses are columnar and the others polygonal. The central parts of the epithelial masses tend to degenerate and to be replaced by fibrin or calcareous tissue. The appearance suggests that many of the spaces are formed in this way by disintegration of the tumour.

Case 2.—F. S., aged 35, female, was admitted to the National Hospital, under Dr. Gordon Holmes, on November 29, 1919, complaining of blindness, headache and adiposity. She gave the following history of her illness. Fifteen months previously amenorrhœa commenced; then she began to get fatter, felt tired, and about the same time noticed a slight alteration in her sight. Vision became worse nine months later and occasionally she had diplopia. During the last two weeks vision had deteriorated very much and light irritated her eyes so that she wanted to keep them closed. She had suffered from slight headaches for a long time, especially in the mornings, but they had become much worse during the past month and had been accompanied by vomiting for the last week. She thought that she passed more urine than formerly.

At the beginning of her illness she weighed 11 stone.

Examination.—An enormously fat, but otherwise healthy looking woman, weight 16 st. 6 lb. Her skin was fairly fine, but very dry and soft. There was no alteration in the body hair except perhaps that it was somewhat sparse, but the hair of her head was thick and normal in appearance and quality.

No loss of sense of smell detected. Visual acuity of the left eye was $\frac{6}{60}$ and that of the right even less.

Perimetric examination revealed a partial scotoma for white in right inferior quadrant of right eye, and indistinctness of vision in the rest of the temporal field. No scotoma for white was detected in the left eye.

She was unable to recognize red or green in the region of the fixation point in either eye, but her headaches were so severe that complete examination was not possible. Her optic discs appeared normal. Her right pupil was slightly larger than left; both were circular, and reacted to direct and consensual illumination. There was complete paralysis of right external

rectus, the other ocular muscles being normal, but the left eye developed nystagmoid jerks on looking to the right. No abnormalities were detected in the functions of the other cranial nerves, and the motor and sensory systems and the reflexes were normal.

Her systolic blood-pressure was 121 mm. Hg, the diastolic being 82 mm. Hg.

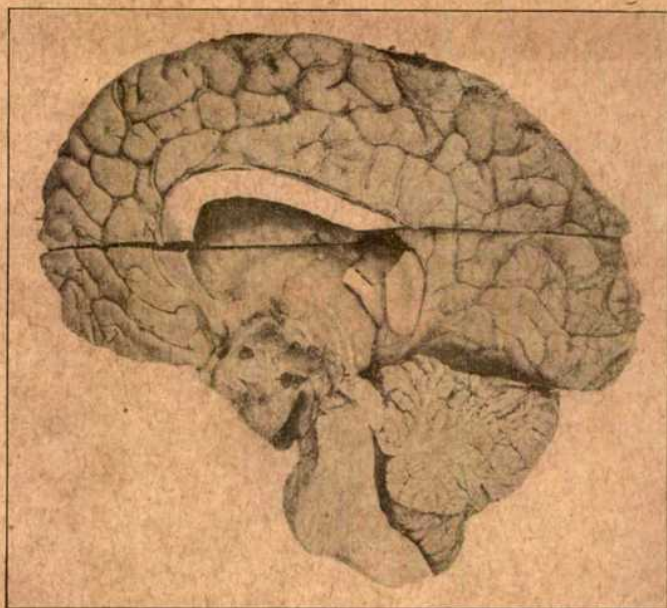


FIG. 3.—Case 2. Mesial sagittal section through brain showing right half of tumour in position.

Radiographic examination showed no evidence of enlargement of the sella turcica in the antero-posterior plane, but viewed stereoscopically it appeared enlarged laterally. The sugar tolerance was not above normal, 100 grm. of glucose giving rise to glycosuria.

On January 24, 1920, a right temporo-parietal decompression operation was performed by Mr. Percy Sargent; there were evidences of an enormous increase of intracranial pressure. Patient died five days later.

Pathological investigation.—A post-mortem examination was made on the day after death. On removal of the brain a tumour about the size of a walnut was found in and above the sella turcica. It lay slightly to the left of the mid-line, behind the chiasma which it had pressed forward. In a sagittal section through the brain the tumour was seen to be semi-cystic, and to be attached to the floor of the third ventricle throughout its whole length (fig. 3).

There was very great enlargement of the pituitary fossa, chiefly at the expense of its anterior margin. The posterior clinoid processes were also pushed backwards.

On microscopical examination the tumour tissue is seen to be composed of branching epithelial masses of various shapes projecting in all directions and enclosing cystic spaces (fig. 4). Some of these cystic spaces contain a serous looking substance, and others organizing fibrinous matter. Calcareous deposits are also found within them. The cells of the outer layer of the

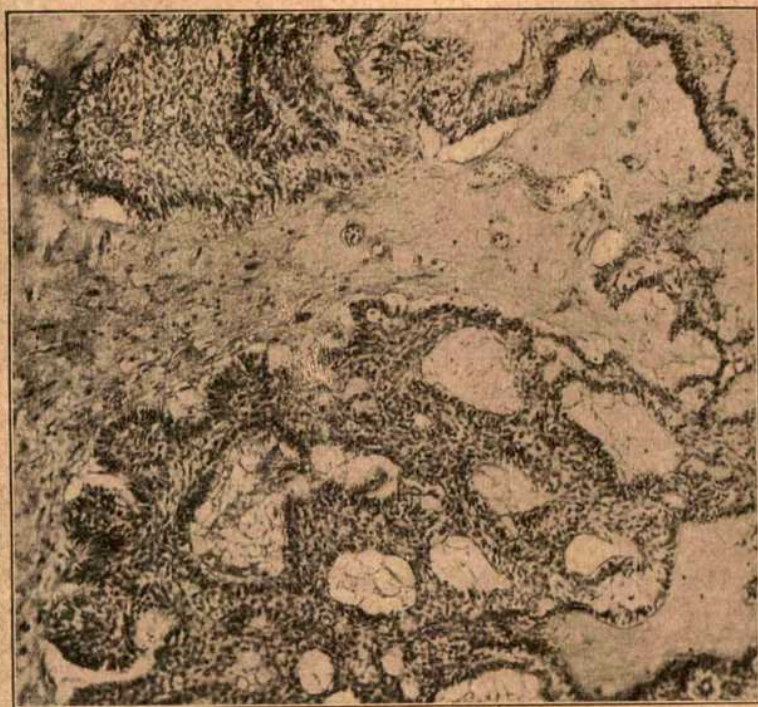


FIG. 4.—*Case 2.* Photomicrograph of section of that part of the tumour adjacent to the infundibulum showing branching epithelial masses enclosing cystic spaces and neuroglial tissue intervening between the epithelial processes.

epithelial masses which are in contact with these spaces are columnar and the more centrally placed are polygonal. Occasionally in the central area of some of the strands the cells are flattened. In that portion of the tumour adjacent to the brain there is a large amount of glial tissue intervening between the branching cellular processes. The blood-vessels are scanty and thin walled, they lie within the spaces and tend to channel the epithelial strands.

Case 3.—W. L., aged 18, female, was admitted to the National Hospital under Dr. Farquhar Buzzard, on February 12, 1920, complaining of headache

and loss of sight. Although 18 years of age she had never menstruated. Two years before admission she had begun to complain of frontal headaches which were worse each morning. She did not suffer from vomiting until twelve months before admission when it commenced accompanying the headaches and having no relation to food. About two months after the headaches began her vision became blurred, so that she could neither see to read nor to thread a needle. Her mother stated that at first she used to bump into people who were walking at her side as she could see only in front of her, and that she had to turn her head to look to either side. She had always been fat; before Christmas, 1919, her face assumed a bloated appearance, but this had become less pronounced. She was rather drowsy and was always dropping off to sleep.

Examination.—The patient was a very fat girl of 18 years who appeared to be only 12 to 14 years of age; she had a childish voice, and was of cheerful disposition. Her skin was abnormally dry and scaly. There was very little body hair, only two to three hairs in the axillæ and very few over the pubis, but the hair of her head was fairly long, thick and silky.

No loss of sense of smell was detected. Visual acuity was so diminished that she could only appreciate coarse hand movements. It was impossible to test her visual fields owing to failure of sight. Ophthalmoscopic examination revealed primary optic atrophy in both eyes. Her pupils were widely dilated, the left being slightly larger than the right. No reaction to light nor to accommodation was obtained in either. Both external and both internal recti were weak, and there was a divergent squint which became a little less marked when she tried to converge. No abnormalities were detected in the functions of the other cranial nerves, and the motor and sensory systems and the reflexes were normal.

The heart, lungs and alimentary system presented no marked abnormalities. The systolic blood-pressure was 100 mm. Hg, the diastolic being 70 mm. Hg. Sugar tolerance: 100 gm. of glucose given orally did not produce glycosuria. Other tests with larger quantities of glucose failed, as the patient vomited. Radiographic examination showed that the sella turcica was much larger than normal.

An operation was undertaken on March 20, by Mr. Percy Sargent. After a frontal osteoplastic flap, hinged in the temporal fossa, was made the frontal lobe was elevated and the tumour reached. A large quantity of yellow fluid containing numerous shimmering cholesterol crystals was removed from it by aspiration. After the operation the patient became almost maniacal, talking incessantly, was very restless and tried to get out of bed. A few days later her temperature began to rise and reached 106° F. An urticarial rash appeared on the back and buttocks. A lumbar puncture was performed and no evidence of meningitis was found. She died on April 2.

Pathological investigation.—A post-mortem examination was made on the following day. On lifting the frontal lobes of the brain, a tumour about the size of a walnut was seen filling the sella turcica with the optic nerves stretched

over it. The sella turcica was appreciably enlarged laterally and antero-posteriorly but was not abnormally deep. An attempt was made to dissect the tumour from the surrounding tissues but in doing so the cyst burst and much brownish fluid with numerous plate-like crystals of cholesterin escaped. A few large solid masses of crystals were also found within it, and one plate of hard calcareous matter was seen attached to the upper wall of the cyst. In a sagittal section through the brain the tumour was seen to lie in the mid-line. The wall of the cyst was firmly attached to the floor of the third ventricle and to the infundibulum from which it apparently had arisen (fig. 5).

A portion of the cyst wall examined microscopically was seen to be formed of fibrous tissue only; no epithelial cell masses could be detected in it.

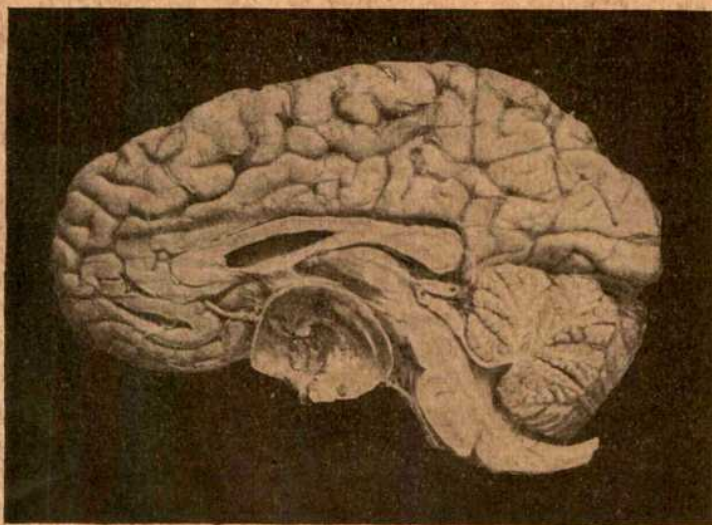


FIG. 5.—Case 3. Mesial sagittal section through brain showing right half of cyst in position.

In the first two cases described above the semi-cystic tumours were apparently of the same nature. The tumour tissue was composed of nests and branching masses of epithelial cells, enclosing cystic space the serous content of which was in the process of organization. The epithelial masses were made up of several layers of cells; the basal layer being composed of columnar cells while the cells of the superimposed layers were chiefly polygonal. This epithelial tissue appeared to originate by the proliferation of the ependyma lining the recesses of the infundibuli. In fact this was fairly definitely shown in the first case. The calcareous deposit seen within the cystic spaces seemed to have

been formed as a result of degenerative changes having taken place in the organized tissue within the spaces.

This type of tumour cannot be regarded as being entirely encapsuled, for in Case 1 there was evidence of its extension into the brain tissue near its place of origin.

Similar solid or semi-solid epithelial cell tumours occurring in relation to the infundibulum and third ventricle have frequently been described. The tissue from which this type of tumour originates has always been a matter of some speculation. Mott and Barratt [15] describe two cases, one of which they assumed originated from the choroid plexus, or from the lining epithelium of the infundibulum or of the third ventricle which it filled. Another, which resembled a papilloma, they regarded as an epidermoid cyst developed from misplaced ectodermal cells intended to form the scalp. Here the epithelial structure of the neoplasm bore a very close resemblance to the rete Malpighii of the skin, although no hairs nor fatty matter were present. Langer [10] also described two cases of papillary cysts which he regarded as definitely of infundibular origin.

Hecht [7], in 1909, described a tumour which very closely resembled the tumours in Cases 1 and 2, except that it contained some typical osteoid tissue which, however, may have been a fragment of the sella turcica, since the bone here was markedly corroded and thinned out. In a case described by Otto Kankleit [9], a remnant of the eroded wall of the sella turcica was found in the tumour. The parenchyma of the tumour described by Hecht was considered to have been formed by proliferating cells of the pars anterior of the pituitary body. The cells formed alveoli-like spaces in a stroma of very loose vascular embryonal connective tissue composed of stellate cells. These alveoli were either completely filled with epithelial cells, or there was present only an outer shell of epithelial cells and an inner mass of hyaline material. The tissue in the interior of the spaces looked somewhat like "epithelial pearls" of cornifying carcinomata, although the material did not show any true cornification. The epithelial cells forming the follicular spaces were cuboidal or short columnar cells. These cells had not only formed alveolar spaces but had also proliferated in a very irregular manner, so that this had led to the formation of irregular masses and tracts of cells. The hard portions of the tumour were composed of very coarse connective fibrils and fibril bundles which were infiltrated with lime salts. Other parts contained all the osseous elements of bone, corpuscles, Persian canals, concentric lamellae and cellular marrow spaces.

Where the tumour was fused with the floor of the third ventricle there was a loose oedematous connective tissue with numerous coarse and delicate wavy fibres forming a wide-meshed reticulum. Dorsal to it was seen a portion of the choroid plexus, the ependymal cells of which had proliferated and formed branching villous excrescences. No cartilage was found in the tumour nor any glia cells or fibres. Hecht regarded this tumour as belonging to that type of teratoma which imitates an entire embryonic region.

The other tumours similar in structure to those of Cases 1 and 2, and which the writers regarded as having possibly originated from the third ventricle, were described by Lereboullet, Morizon and Cathala [11], and the other by Claude and Schaeffer [1]. Cushing [2], Wilfred Harris and Cecil Graham [6], have also recorded cases of cystic epitheliomata of the infundibulum and third ventricle.

Erdheim [3] in 1904 described seven personally observed cases of tumour which he considered to have arisen from "rests" of that part of the ectoderm of the original embryonic buccal cavity which goes to form the cranio-pharyngeal duct. A part of this lies during its final development in the region of the infundibulum and the upper surface of the anterior lobe of the pituitary, and he demonstrated the frequency with which "rests" of the duct occur in this situation by finding them in ten out of thirteen fetuses examined. These tumours are described as being always in the mid-line and generally originating in the infundibulum. Some were solid but the greater number were cystic and contained a serous fluid in which cholesterol crystals were frequently found. The tumour tissue is described as being epithelial and the cells as resembling those of the buccal mucosa. Both macroscopically and microscopically these tumours appear to resemble very closely the first two described above. Various other observers have followed Erdheim in considering such epithelial tumours to have been derived from the cranio-pharyngeal duct, basing their conclusion partly on the structure of the tumour and partly on its situation.

One of the most striking examples was that described by Farnell [4]. This was a tumour about the size of a golf-ball occurring in the usual situation, in the mid-line and behind the optic chiasma. It had an adeno-papillomatous structure. The remarkable feature of the tumour was that the epithelial tissue not only resembled the buccal epithelium but even the mandibular type of epithelium composing the enamel-forming organ of the tooth. Hence Farnell regards the tumour not only as a hypophyseal cholesteatoma, but also as an adamantinoma.

comparable to the tumours which develop in the jaw from the dental epithelium. All these cranio-pharyngeal tumours, however, do not present such a typical form of epithelioma. Many of them have been described as being papillomatous, with flat-celled epithelium, and sometimes as containing apparently isolated cell-nests. They thus resemble very closely the structure of the tumours of the first two cases described in this paper. Such neoplasms have also been reported by Harms [5], Kankaleit [9], Mackay and Bruce [14], Strada [18], Lewis [12], and Harry Jackson [8].

The cyst in Case 3, the wall of which contained only fibrous tissue, is evidently of a rarer type. Except that it apparently originated from the infundibulum, its origin is obscure.

There is no doubt that growths of an epithelial nature are the most frequent type of supra-pituitary tumour. Other types of tumours which have occurred in this region are two instances of teratomata and one of an endothelioma described by Cushing [2]. Lockwood [13] records a typical cholesteatoma, Silfvast [17] a glioma and an endothelioma. A case of myxo-chondro-sarcoma was published by Mott and Barratt [15], who also report a very rare instance of mycotic infection which, by irritation, had set up a new growth in the supra-pituitary region.

These tumours occurring in the supra-pituitary region generally produce fairly constant local and general symptoms. The chief local symptoms are those due to involvement of the chiasma and optic tracts, generally producing a bitemporal hemianopsia, and eventually total blindness with optic atrophy if the tumour is not partially removed by operation. In a late stage of the disease there is often increased intracranial pressure, brought about mainly by interference with the escape of cerebrospinal fluid from the lateral and third ventricles. The general symptoms, however, are much more interesting; they generally approximate to the type of dystrophia adiposo-genitalis described originally by Fröhlich. The outstanding symptoms are adiposity, with a feminine type of fat distribution over chest, abdomen, hips and thighs, and either non-development of the secondary sex characteristics if the condition had occurred before puberty, or some loss of them if the condition had commenced after puberty. Hence in cases in which the disease begins in childhood, the genital organs always remain infantile; the pubic and axillary hair never becomes more than very scanty, and in girls menstruation is never established. When the condition sets in after puberty has been established, cessation of menstrea-

tion in women and impotence in men are early symptoms, and the genital organs gradually revert back to pre-adolescent state. There is a very decided diminution in the body hair; the axillary hair often disappears altogether, that over the pubes becomes very scanty. The beard and moustache become thin, or the patient may not need to shave so frequently as previously, although the hair of the scalp does not seem to be affected. The skin of these patients is generally very dry, and extremely smooth and delicate. Metabolism is often, though not always, deranged. Frequently there is an increased carbohydrate tolerance. In other cases, such as those reported by Newmark [16] and by Cushing [2], an outstanding feature was diabetes insipidus. Low blood-pressure, epileptiform seizures, and lowered mentality may also occur. The cause of these striking symptoms has been the subject of much investigation. On account of the involvement of the pituitary gland by pressure of these supra-pituitary tumours, the symptoms have been generally attributed to a diminished secretion of the hypophysis. This theory of hypopituitarism as the cause of Fröhlich's syndrome has been strongly supported by the experiments by Cushing upon dogs. He found that puppies deprived of all their pituitary gland, except a fragment of the pars anterior, became adipose, their sugar tolerance was increased, they remained sexually infantile, and skeletal growth was very greatly retarded. Similar experiments upon adult dogs produced adiposity, increased sugar tolerance, and reversible sexual changes. Further, he observed that animals deprived of only the posterior lobe of the pituitary gland acquired a high sugar tolerance and became very fat, and that intravenous injection of posterior lobe extract produced glycogenolysis, and its continued administration in excessive amounts leads to emaciation.

The exact relation of polyuria and polydipsia to the pituitary gland is still somewhat uncertain, but its occasional occurrence in tumours in the pituitary region indicate that the relation is a close one. Newmark [16] has described a case of severe diabetes insipidus, in which a tumour occupying the region of the infundibulum was found to have destroyed the pars nervosa and most of the pars intermedia. The second case described in this paper had polyuria. It would, therefore, appear as if a destructive lesion of the pars nervosa might result in polyuria. On the other hand, the oral administration of posterior lobe substance in animals had been observed by Schäfer to have a diuretic effect.

There is, therefore, much evidence correlating the state of dystrophia

adiposo-genitalis presented by cases of supra-pituitary tumour with the damage or destruction of the gland. It is also possible that the normal discharge of the posterior lobe secretion into the third ventricle via the infundibular cavity may be interrupted by the involvement of the infundibulum by the tumour. On the other hand, Erdheim believes that the Fröhlich syndrome may be caused by the growing tumour interfering with certain centres at the base of the brain apart from the pituitary gland.

A perusal of the literature on the subject of supra-pituitary tumours shows that about 70 per cent. of these tumours are associated with Fröhlich's syndrome.

The writer is indebted to Dr. Gordon Holmes and Dr. Farquhar Buzzard for permission to publish their cases, and to Dr. Godwin Greenfield for taking the photographs which illustrate this paper.

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THE NERVOUS CONTROL OF THE URINARY BLADDER IN AMPHIBIANS.¹

BY F. J. F. BARRINGTON.

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THE experiments described in this paper were undertaken to determine whether the normal evacuation of the urinary bladder in amphibians depended on the integrity of some part of the anterior end of the hind-brain, as has previously been shown to be the case in the cat [1].

The animals used were the common frog (*Rana fusca*), the common toad (*Bufo vulgaris*), the crested newt (*Molge cristata*) and the spotted salamander (*Salamandra maculosa*).

Various proportions of chloroform and ether dissolved in water were tried for the anæsthetic. One c.c. of ether to 100 c.c. of water appeared to be the best, and this mixture was used in the majority of the experiments. The animals were put in a closed glass vessel containing such a quantity of this mixture that they were not completely submerged, and left there till all reflexes, including respiration, were abolished. Though given no further anæsthetic they did not come round till a considerable time after the operation was finished.

After operation the animals were kept till they were killed in a sink into which water was slowly dripping; the surface of the sink was therefore always wet but there was not sufficient water in it to cover them. Most of the animals were kept two days after operation; they were then killed with ether water, the abdomen opened and the degree of distension of the bladder noted. This can easily be determined in frogs during life by a translucent area in the region of the bladder; the same applies to the other animals if a strong light is used. From observations it seems that two days was an unnecessarily long time, probably the same results would have been obtained if the period had been one day.

¹ The expenses of this research have been defrayed by a grant from the Dixon Fund of the University of London.

THE EFFECT OF REMOVAL OF PARTS OF THE BRAIN.

Portions of the brain were removed in anæsthetized animals by removing part of the roof of the skull, dividing the brain transversely and scooping out the part anterior to the section; the skin incision was then closed. The actual position of the brain transection was determined after death and hardening in formalin by naked-eye examination.

These experiments were made on fourteen frogs, length between 5 and 7 cm.; five toads, length between $6\frac{1}{2}$ cm. and 9 cm.; eight newts, length between $11\frac{1}{2}$ cm. and $14\frac{1}{2}$ cm.; and eleven salamanders, length between $11\frac{1}{2}$ cm. and $15\frac{1}{2}$ cm.

When killed the animals fell into two groups according to the appearance of the bladder; in the one it was tensely distended and marked abdominal distension was present, and in the other, even though containing a considerable amount of urine, its surface always had a crenated appearance; in no case was there ever the slightest doubt into which of these two groups to place an individual animal. Measurements of the bladder contents, though unnecessary, were in most cases attempted by delivering the bladder through an abdominal incision and opening it over a measure. In the case of the frog the figures obtained by this method probably give a fairly accurate idea of the degree of distension. In the toad and salamander the figures usually represent less than the actual degree of distension in the case of distended bladders, since in opening the abdomen a large amount of fluid often escapes from the cloaca. This appears to be due to the absence of a wax skin like that of the frog. In the newt the bladder is so small that the drops adhering to the opened bladder, sides of the measure, &c., may form an appreciable proportion of the bladder contents. In the frogs the normal maximum quantity of urine that can be collected in this way is probably under 2 c.c.; the amounts collected in those with over-distended bladders varied from $3\frac{1}{2}$ c.c. to 12 c.c. In the toad the normal maximum appears to be up to 10 c.c.; the amounts collected in those with over-distended bladders varied from 10 c.c. to 59 c.c., in these a considerable quantity was known to have been lost. In the newt the quantities collected from those with over-distended bladders varied from 0.3 c.c. to 1.2 c.c., and in the salamander from $\frac{1}{2}$ c.c. to $11\frac{1}{2}$ c.c.

Removal of the fore-brain only, with one exception, was never

followed by an over-distended bladder; the exception was a salamander and after hardening the mid-brain was found to have become softened. In all cases where the transection was behind the cerebellum an over-distended bladder resulted. With the exception of one newt, on which not much reliance can be placed on account of the small size of the brain, all cases where the transection went between the cerebellum and the mid-brain resulted in an over-distended bladder. With the exception of one frog in which the whole mid-brain was found to be softened, no experiment resulted in an over-distended bladder where the transection was made through the anterior half of the mid-brain. A transection through the posterior half of the mid-brain was only made in one frog and in it the bladder was not over-distended. If therefore, as is probable, the result in the newt alluded to was an error in observation, the over-distended state of the bladder observed in all four species is due to the destruction of some part of the posterior half of mid-brain.

This localization approximates to that already described in the cat as nearly as could be expected from the methods employed in the two cases. In the cat, however, paralysis of the bladder was shown to be present; in the amphibian the over-distension might be due to this or to failure of the closing mechanism to relax. A third possibility arises from the fact that the ureters do not open directly into the bladder, namely, that the over-distension might be due to some abnormal rate of filling of the bladder. This, however, cannot be the explanation, since in normal frogs it is quite easy to see that the bladder is emptied when urine is passed by the disappearance of the translucent area in the bladder region, whereas in animals with over-distended bladders, even though considerable quantities of urine may escape during struggling when the animal is handled, a large translucent area in the bladder region persists. Though there is no direct proof that the failure of the bladder to empty is due to its paralysis, it seems unlikely that it is dependent on a tonic contraction of the sphincter from the fact already stated that in animals with over-distended bladders comparative slight mechanical causes can lead to the expulsion of considerable quantities of urine from the cloaca, though the bladder is still over-distended at the end.

THE EFFECT OF DIVISION OF THE SPINAL CORD AND OF THE SPINAL ROOTS.

(a) *In the Anura.*

Division of the spinal cord in frogs, the species of which is not stated, was found by Exner [3] to lead to great dilatation of the bladder; the level of transection was stated to be at the fourth or fifth vertebra, but it is not given in relation to spinal roots. It was shown by Gaskell [4] that the bladder of the frog, as of the mammal, has a double innervation, the anterior fibres reaching it by the sympathetic and the posterior, which correspond to the pelvic nerve of mammals, arising directly from the sciatic plexus. The spinal roots from which contraction of the bladder could be elicited in the frog were found by Horton Smith [5] to be the ventral roots of the seventh, ninth and tenth, but not of the eighth; the seventh required a stronger stimulus to obtain the effect than the ninth or tenth. Dale [2] showed that in the toad stimulation of the same roots, the seventh, ninth and tenth, and of these only, gave rise to contraction of the bladder.

In the experiment about to be described the first root is considered to be the one emerging between the first and second vertebrae. In many experiments on frogs and toads the lower roots are counted from the posterior end and errors are therefore liable to occur if there is a variation of the normal root arrangement. In the urodela the levels of lesions are given in vertebrae; as the roots emerge from the spinal canal directly they arise from the cord this is not open to objection.

Division of the spinal cord at various levels from the second to fifth roots was performed in six frogs and four toads; in some experiments the cord posterior to the transection was excised, in some it softened and in others it functioned, reflex movements of the hind limbs being obtainable. In all these cases great over-distension of the bladder resulted. The nervous impulse which leads to the normal emptying of the bladder must therefore travel from the posterior half of the mid-brain down the anterior half of the spinal cord.

In two frogs the cord was divided behind the seventh roots and no normal distension of the bladder occurred. Division of the ninth and tenth spinal roots was performed in three frogs and five toads; over-distension of the bladder did not result in any case. The toads usually had full bladders when killed but they were always within the normal limits: in the three frogs the bladders were nearly or quite empty. At

any rate the whole mid-brain effect cannot act through the posterior spinal nerves. This appeared such a fundamental difference from the condition in the cat that it was thought the mid-brain influence might be masked by a possible paralysis of the sphincter of the bladder. This was shown not to be the case by dividing the ninth and tenth roots and the cord between the second and third roots at the same operation. flexion of the hips and knees could be obtained then by touching the toes and an over-distended bladder resulted.

Division of the lower spinal roots, excepting the last two, is a difficult operation in the frog and toad, and not an easy one to control by dissection two days after it has been done. It was attempted by removing the laminæ of the four hindmost vertebræ and dividing all roots exposed which emerged in front of the ninth vertebra on both sides. In this way the sixth, seventh and eighth roots were usually divided and the ninth and tenth left intact. In three frogs there was over-distension of the bladder after this operation, but in these there was complete paralysis of all movements of the limbs, including the toes: the ninth and tenth roots, though not actually divided, were therefore not functioning. In one frog in which this operation had been performed, and the ninth and tenth roots of one side divided as well, there was no over-distension of the bladder, but voluntary flexion of the toes of the opposite side occurred during life. In two other frogs, where the sixth, seventh and eighth roots had been divided on both sides, there was no over-distension of the bladder; movement of the toes was seen in one, but in the other no observations were made on this point. In two other frogs the seventh root on both sides, and the seventh and eighth on both sides, were divided and no over-distension of the bladder resulted. Division of the seventh root in frogs does not, therefore, lead to over-distension of the bladder if the ninth and tenth roots are intact even on one side. One experiment only was an exception to this and does not seem easy to explain: an over-distended (8 c c) bladder was present in a frog: anatomical examination showed the ninth and tenth roots intact, and the sixth and seventh roots divided on both sides, the eighth root was intact on the right side, and its dorsal root only divided on the left side: during life there was paralysis of the whole left hind limb except for movement of the toes, but flexion of the joints of the right hind limb occurred. The sixth, seventh and eighth roots were divided in one toad: paralysis of both hind limbs except for the toe movements resulted, but there was no over-distension of the bladder.

In the frog and toad, therefore, both the anterior and posterior sets of roots must be divided to produce over-distension of the bladder; from this it follows that the impulses from the posterior part of the mid-brain which normally prevent over-distension must pass out through both sets of nerves.

(b) *In the Urodela.*

In two newts division of the cord at the eighth and at the tenth vertebræ respectively resulted in an over-distended bladder.

The nerve roots supplying the bladder in the salamander are apparently not known. Only one experiment was made on this animal. The brain having been destroyed, the laminæ of the eleventh to the eighteenth vertebræ were removed; the cord was damaged in doing this, and it was divided at the level of the twelfth vertebra. It was then stimulated with a unipolar electrode at the posterior border of each vertebra, from the twelfth to the eighteenth inclusive, for about ten seconds; contraction of the bladder occurred when the stimulus was applied at the lower border of the seventeenth vertebra but nowhere else. An attempt was then made to divide this part of the cord into segments and the stimulation repeated with the same current (Kr. 400); the contraction again only occurred at the seventeenth. The stimulus was then increased and the experiment repeated twice again; a marked bladder contraction resulted at the seventeenth vertebra on both occasions and a doubtful one at the fifteenth on one. In this salamander the large roots to the hind limb plexus were the fifteenth, sixteenth and seventeenth; the seventeenth root therefore corresponds to the ninth in the frog and toad. The experiment does not show whether an upper set of nerves exists, and if so where it is, but it is sufficient to show the main part of the lower set arises from the posterior part of the hind limb plexus as in the frog, toad and mammal.

In three salamanders the cord was divided and in all an over-distended bladder resulted. In one the level of transection was the thirteenth roots, the fourteenth being the most anterior large root to the hind limb plexus. In the other two the level was the sixteenth root, the fifteenth and sixteenth respectively were the first large roots to the hind limb plexuses. It is therefore probable that if an upper set of bladder nerves exists in the salamander only the lower set convey impulses from the posterior part of the mid-brain to the bladder, in which case the salamander differs from the frog and toad in this respect and resembles the cat.

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Some Varieties of Traumatic and Toxic Ulnar Neuritis.

By E. FARQUHAR BUZZARD.

MY interest in the ulnar nerve was first excited in a very personal manner about twenty-five years ago. Having succeeded during the course of a hospital football match in fracturing one of my collar bones, my arm was duly fastened to my chest in a position of extreme flexion at the elbow with results which still live vividly in my memory. After a very few hours I began to experience discomfort in the sensory distribution of the ulnar nerve. At the end of a couple of days the pain and paræsthesia were so intense that I was obliged to beg for the release of my arm from its fixed position. It is quite true that many persons are able to submit to the same procedure without experiencing any discomfort, and it would seem that some anatomical peculiarity was responsible for my distress. At the same time this peculiarity is shared by a good many people, some of whom complain that if they sleep with an arm flexed, they are liable to wake with paræsthesia referred to the distribution of the ulnar nerve.

NEURITIS WITH NO OBVIOUS ANATOMICAL FEATURE.

With this introduction I may refer at once to the first group of cases of ulnar neuritis to which I would like to draw your attention. In this group there is no obvious anatomical feature which can be taken as a factor in the production of the neuritis. Examination of the nerve at the elbow does not reveal any abnormality in regard to its relations with bony structures, and it lies well protected in the ulnar groove. The complaint may be limited to a transient disturbance

of function as a result of the excessive use of the hand and arm in a flexed position. A good example of this was the case of a lady, aged 33, who complained of complete failure of function on the part of the two ulnar fingers of the left hand occurring on several occasions at the end of a long 'cello recital. She had played the 'cello since she was 5 years of age, and had recently indulged in what may be regarded as excessive hours of practice. But it is possible to produce more permanent ulnar disturbances by excessive use of an arm, as in the case of a man who came to me complaining of numbness in the ulnar fingers of the right hand and slight pain in the region of the elbow. On examination, there was found some loss of epicritic sensibility in the ulnar distribution and slight atrophy and weakness of the ulnar muscles, including flexor carpi ulnaris. At the elbow the nerve seemed to be in good position, and the only abnormality found was slight tenderness just below its exit from the ulnar groove. This condition had apparently been produced by a long spell of fishing with a heavy salmon rod, and any attempt at using a rod or a tennis racket sufficed to renew the pain, and was attended with difficulty in maintaining a proper grasp.

Even less violent exertions may sometimes end in a similar condition. For instance, a lady, aged 43, complained that for three weeks she had had difficulty in using her right hand, and was conscious of a pain like a sting in the ulnar border of the palm and in the two ulnar fingers. The ulnar muscles were obviously weak, but showed very little atrophy, and no definite sensory loss could be detected. The only aetiological factor which I could discover in her case was a period of excessive use of the hand in sewing and writing.

CASES WITH AN ADDITIONAL TOXIC FACTOR.

Closely allied to the group I have just described is another in which it is possible to find an additional aetiological factor in the form of some toxic agent. In these cases, again, no anatomical abnormalities can be detected, and the most characteristic feature of this form of ulnar neuritis is its onset, while the patient is confined to bed with some infective or septic illness. I saw quite a number of cases of this description during the war, especially among soldiers confined to bed with severe compound fractures and subsequent prolonged sepsis.

Captain G. M., aged 21, sustained a wound of the right leg, which was amputated. He was laid up for three months in bed with septic conditions, and after about two or three weeks noticed increasing numbness

soreness in the ulnar fingers of both hands. The right hand recovered in the course of five weeks, but the left hand showed atrophic palsy of the ulnar muscles, with some sensory impairment in the ulnar cutaneous area.

I am inclined to attribute the ulnar neuritis in these cases partly to the fact that the arms are constantly being used in the flexed position—partly, perhaps, to an undue amount of friction, and partly to the effect of some toxic agent. In civilian life I have seen a precisely similar condition arising bilaterally in a patient who had been in bed for a fortnight with a slight attack of small-pox. All the cases of this kind which I have come across have made a good recovery. Perhaps one ought to include in this group the occasional case of ulnar neuritis associated with glycosuria, and others in which the only ætiological factor of importance appears to be the gouty diathesis. An interesting example of the latter was a patient, aged 61, who came to me complaining of pain in the ulnar fingers and ulnar aspect of the left hand which had come on suddenly eight months previously after sitting out one evening in the garden. I found definite, but slight, wasting of the ulnar muscles and slight impairment of sensibility in the ulnar area. He suffered from gouty eczema, a gouty big toe, and presented gouty deposits in the lobe of the left ear.

CASES WITH SOME ANATOMICAL PECULIARITY.

My third group of cases comprises those in which some anatomical peculiarity can be discovered in connection with the relations of the nerve at the elbow. These cases may be subdivided into: (1) those with a history of severe injury to the elbow; (2) those without any history of trauma.

(1) It has long been recognized that ulnar neuritis may develop many years after an injury to the elbow, and this condition has been ascribed to involvement of the nerve in callus or in fibrous adhesions. I have seen a number of cases of this kind, and the outstanding feature has always been the unprotected position of the nerve at the elbow. It would seem that in these cases the nerve is constantly exposed to minor insults and injuries, each one of which may produce very little immediate effect, but which in the aggregate lead to the formation of a fibrous neuroma. This neuroma is generally a fusiform swelling of the nerve due to a large increase of its connective tissue elements. I have seen no evidence of bony pressure, and fibrous adhesions to surrounding structures are rarely prominent. On the other hand, constriction of the nerve is not very uncommon.

Mrs. O., aged 30, gave me a history that two and a half years before our interview she had sustained a violent blow on the right elbow with a tennis racket and that some months later she began to find slight difficulty with her right hand. She was unable to play tennis or use the arm in any strenuous way during the following summer. She complained of pain in the elbow even when writing or using a needle, and I found the nerve at the elbow very easily displaced and over-exposed. It was tender on palpation and there was some impairment of sensibility in its distribution. Mr. Wilfred Trotter placed this nerve in front of the joint in March, 1920, with the result that the patient is now able to use her hand and arm without any discomfort or disability.

Mrs. S., aged 45, gave a five years' history of wasting and weakness of the left hand with slight pain at the left elbow and in the ulnar side of the hand. She displayed almost complete ulnar palsy as regards the intrinsic hand muscles and some weakness of flexor carpi ulnaris. There was only slight sensory disturbance. The nerve at the elbow was thickened and exposed. In this case there was a history of fracture of the left arm at the elbow forty-two years previously. Mr. Trotter operated and found a spindle-shaped neuroma of the nerve at the elbow, and contented himself with transposing it in front of the joint.

(2) There appear to be a number of people whom nature has treated rather shabbily in regard to protection of the ulnar nerve at the elbow. The groove is very shallow, and when the elbow is passively flexed the nerve can be felt to slip out of it and to lie in an exposed position over the inner condyle. These people may escape any serious consequences of their anatomical peculiarity unless circumstances necessitate a more or less strenuous and continued employment of their arms.

A very good example of this type of case was provided by a man, aged 46, who was sent to me complaining of weakness and wasting in the left hand, and with a sensation of numbness on its ulnar side during a period of about four months. On examination I found a very poor ulnar groove and a large thickened nerve easily palpable on the surface of the bone; there was almost complete atrophic palsy of the ulnar muscles, including flexor carpi ulnaris, and partial sensory loss in the ulnar distribution.

The chief exciting factor in this case appeared to be the fact that the patient spent his time driving a two-horse van with his left arm. A possible accessory factor may have been a somewhat excessive consumption of beer. Mr. P. Sargent operated on this patient and found a fusiform swelling involving the whole thickness of the nerve for a three-quarters of an inch. Below this neuroma the nerve passed beneath a dense fibrous archway which constricted it.

I have seen many other cases of this kind, and a very interesting example was the following:—

A platelaver was in the habit of swinging a heavy hammer impartially with both arms. When I saw him he was complaining of atrophy and weakness of the muscles of both hands characteristic of an ulnar lesion. Both ulnar nerves were unusually unprotected and mobile at the bend of the elbows and each exhibited a large diffuse neuroma.

This case afforded a good example of difficulty in diagnosis in that he complained of no pain and but little paræsthesia in his hands. Except for the limitation of the atrophy to the muscles supplied by both ulnar nerves, he would have passed for a case of progressive muscular atrophy, the diagnosis with which he arrived in my out-patient room. It is worthy of note that the sensory disturbance in these patients varies very much, but on the whole is less severe than the motor palsy and muscular atrophy.

DIFFERENTIAL DIAGNOSIS.

A careful examination should suffice in all cases to distinguish an ulnar palsy from a spinal cord lesion in the form of progressive muscular atrophy or syringomyelia. On the other hand, so much attention has been paid in recent years to the presence of cervical ribs and the interesting clinical phenomena to which they give rise, that cases of the kind I have been describing are not infrequently sent for X-ray examination on the suspicion that a supernumerary rib may be held responsible for the disability. That such a procedure may give rise to confusion rather than to help in diagnosis is well illustrated by a patient whom I saw two or three years ago and who was ultimately operated on by my colleague, Mr. Cyril Nitch.

He was a man 40 years of age, who, seven years before he came under observation, fell off a motor bicycle and injured his right elbow. He was told that there was no fracture of the bone, but the joint was painful for several weeks and for some time he was unable to straighten his arm. He made complete recovery, but six or seven years later he noticed wasting of some of his right hand muscles and he felt an occasional tingling over the ulnar side of his hand on straightening his arm. This wasting was preceded for some time by a condition of cramp in his fingers when he was writing. On examination there was distinct wasting of the first dorsal interosseous muscle and epicritic sensibility over the ulnar border of the hand was diminished. The ulnar nerve at the bend of the elbow was freely movable and not obviously thickened. This patient had both his elbow and neck X-rayed. The skiagram of the elbow showed an old fracture of the external condyle with downward displacement, but no signs of injury to the internal condyle. The skiagram of the neck revealed a well-developed seventh cervical transverse process on each side and a rudimentary cervical rib on the right. The motor and sensory

disturbance in the hand determined the diagnosis in spite of the cervical rib, and Mr. Nitch exposed the ulnar nerve at the back of the elbow. It was much thickened by scar tissue in the groove behind the internal condyle and was bound down to the latter by firm adhesions attached to its sheath. On palpation the nerve felt tough and fibrous. It was lifted from its bed after dividing the fascia uniting the two heads of flexor carpi ulnaris and was displaced forwards in front of the internal condyle and kept in position by a graft of subcutaneous fat. Within a few weeks the patient had lost all sensory disturbance, and he returned to his work in the East with the intention of continuing electrical treatment to the wasted muscles.

The number of cases which I have very briefly outlined suggests that the ulnar nerve is particularly prone to disturbances of function on what appear to be at first sight slight provocation. Looking for a common factor in these various groups one is struck by the fact that in the majority of cases the ulnar nerve is unprotected by any bony parapet at the bend of the elbow, or so badly protected that during extension and flexion of that joint it is apt to slip in and out of its proper position. During flexion especially it may be exposed to friction and pressure on the internal condyle. A consideration of many cases seems to justify the conclusion that movement, especially of a strenuous and frequently repeated character, is an important factor in the production of an interstitial neuritis. This moving contact with a bony surface is probably an important factor in producing the symptoms associated with a cervical rib, although I do not think it has been shown that in the latter case the nervous tissue becomes surrounded by a definite thickening of connective tissue. In the case of the ulnar nerve, however, the nervous tissue is constantly exposed to minor injuries, and the neuromatous condition so often found must be ascribed to chronic inflammation of traumatic origin. It is a little difficult to understand why the flexed position of the elbow should in itself give rise to discomfort referred to the distribution of the ulnar nerve, as I believe there is no evidence to show that the nerve is stretched by that posture of the limb.

DISCUSSION.

Dr. WILFRED HARRIS said he also had a peculiar interest in the ulnar nerve since the time when, as a schoolboy of 13 years, his left ulnar nerve was struck at the elbow by a stone thrown by another boy. He had great pain at the time and had constantly received minor injuries to his ulnar nerve ever since. He thought that this was one of the disadvantages of the erect position of man, since this posture necessitates frequent acute flexion at the elbow and stretch

of the ulnar nerve. In some of the carnivora the ulnar nerve passes forwards into the forearm through a foramen in the lower portion of the humerus above the joint and is thereby less subject to stretching. There was one point in the distribution of the ulnar nerve which he wished to emphasize. In some cases the ulnar nerve did not supply the first and second dorsal interossei, and in such cases, unless this possibility were realized, a peripheral ulnar lesion might easily be mistaken for a central one.

Dr. STANT BARNES emphasized the nervous origin of the various occupational muscular atrophies. He saw many such cases in his practice in a large industrial establishment, some of them exhibited swellings on the nerve trunks. He instanced a case where a lad, now 17 years old, suffered from a severe ulnar neuritis after a fracture of the internal condyle of the humerus when he was 7 years old. The nerve could be felt running over a promontory, instead of being in a groove. It was difficult to know what to do for this case; every possible measure was tried except operation, and Dr. Barnes' war experience of amputation was not sufficiently encouraging to justify such treatment. Muscular power or sensation remained. Occupational ulnar neuritis was due in many cases to friction between the nerve and the humerus, and the humerus, and the first rib. In a few cases he had seen that friction occurred higher up between the clavicle and the first rib.

Dr. G. RIDDOCH said that the pain resulting from ulnar neuritis due to bone injury could hardly be connected with the involvement of nerve in callus, since it appeared so very late. He instanced a case where the pain came on fifteen months after the injury. This case had proved very difficult to treat. Alcohol injection of the nerve had given relief for one month, and a recent surgical operation had resulted in complete relief for three weeks, but the symptoms were now beginning to reappear. Dr. Riddoch also commented on the fact that some patients exhibited motor and others sensory symptoms following the same sort of injury.

Dr. HENRY HEAD quoted Mr. Sherren's paper on "Neuritis of the Ulnar Nerve, due to Deformity in the Region of the Elbow-joint" (*Edin. Med. Journ.*, June, 1908). In one of these patients the neuroma was excised, the two ends of the nerve sutured, and a fresh groove chiselled in the back of the internal condyle. Voluntary power began to return in sixty-six weeks and all the muscles acted voluntarily in one hundred and thirty-two weeks. Sensibility was also restored. To-day it would be better in such cases to displace the nerve to the front of the internal condyle. Dr. Head also pointed out that the sympathetic supply of the ulnar nerve extended on to the median half of the palm. This was shown by irritative lesions and could be demonstrated in persons by applying a faradic current to the ulnar nerve at the elbow, the tingling extended across the palm almost to the root of the thumb. On the other hand, division of the ulnar caused loss of sensibility over that area assigned in the text-books to this nerve.

The PRESIDENT referred to the delay in the appearance of symptoms after

fracture of the lower end of the humerus. He had seen a clerk, aged 30 years, whose recent ulnar neuritis could only be attributed to a fracture at the age of 4 years. A variety of pathological conditions might be found in these cases. Adhesions were often a cloak for ignorance, but he had in one instance seen a case where the nerve had been compressed under the fibrous arch between the two heads of the flexor carpi ulnaris; complete relief had followed the division of this arch. In another extraordinary case, that of a carpenter who could not flex the elbow beyond a right angle without pain, the nerve was found to be normal at operation, but a loose cartilage was found in a synovial pouch lying between the nerve and olecranon process. The removal of this cartilage cured the patient. For the ordinary type of neuritis associated with a fusiform neuroma, it was his practice to make longitudinal incisions in the sheath, and to transplant the nerve in front of the arm. He agreed that resection of the neuroma with suture of the nerve was quite unnecessary in these cases.

Dr. BUZZARD said he had noticed the occasional abnormal distribution of the ulnar nerve first described by Dr. Harris. The post-traumatic cases could not be due to callus formation, but were due to the more exposed situation of the nerve which resulted from the obliteration of the groove in which it was normally protected, and to the increased amount of movement which resulted from this

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NOTICES OF RECENT PUBLICATIONS

Die Vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen. By Dr. C. U. ARIËNS KAPPERS. II Abschnitt. Mit 320 Figuren im Text und 7 Tafeln. Pp. 705. Haarlem. Bohn. 1921.

The first volume of this book, which was reviewed in a recent number of this Journal, has been quickly followed by the publication of the second and concluding part. Kappers' Comparative Anatomy of the Nervous System of Vertebrates and Man is now complete, and certainly stands without any rival as to the most comprehensive, authoritative and up-to-date textbook on the subject. Lest its title suggest to clinical neurologists and others that it is merely a comparative anatomy and is concerned exclusively with subjects of less immediate interest to them, it must be pointed out that there are few books in which the anatomy of the human brain is so thoroughly and intelligently dealt with.

The first chapter is devoted to the cerebellum, the development of which is traced upwards from its first appearance in petromyzon, where it is merely a correlation centre between the vestibulo-lateral apparatus and more frontally situated mechanisms, to man. Its subdivision, adopted by Kappers, is based largely on the work of his pupil Ingvar, and consequently differs in certain respects from that of Bolk, Elliott Smith and other anatomists, though it is in principle closely allied to them. According to this view the neo-cerebellar parts, to which its increase in size in the higher vertebrates is due, develop in connection with the lobus medius, that part of the vermis which lies between the sulcus primarius and sulcus præpyramidalis, as a result of newly acquired connections with the inferior olives and with the cerebral cortex through the pontine grey matter; while the palæocerebellar components, including the lobus anterior, lobus posterior and formatio vermicularis, remain fundamentally unaltered. An interesting section is devoted to the question of functional localization in the cerebellum, in which the matter is considered from the physiological and experimental as well as from the anatomical point of view.

In the following chapters the midbrain, thalamencephalon, rhinencephalon, corpus striatum and neopallum are dealt with in the same method. One of the most interesting and instructive of these chapters is that which describes the evolution of the corpus striatum and the development of its connections. By following, as the author does, its growth in the succeeding genera of vertebrates, we are enabled to understand not only the rôle it plays in the evolution of the brain, but also the significance of its separate parts and their multifarious and complex connections. This chapter is certainly not easy

reading, but the student who masters it will obtain a better knowledge of the basal ganglia than he can hope to do by any other method of study.

The final chapter is devoted to the neopallium. Here the comparative method has less scope, but the comparison of the different parts of the cerebrum in different genera, and a study of the stages through which each has passed before attaining its final form in the highest vertebrates, throws so much light on structures which we ordinarily know only from a study of human anatomy that we cannot but be grateful to the author for the opportunity which he gives us here of reviewing them in a compact and very readable form.

The volume under review is as copiously illustrated as the first; there are 320 figures scattered through its 705 pages, and in addition seven coloured tables. Specially valuable features of both volumes are the comprehensive bibliographies at the end of each chapter, and the very complete index of subjects and names.

Die neurologische Forschungsrichtung in der Psychopathologie, und andere Aufsätze. By Dr. A. PICK. With 11 Figures in the Text. Pp. 247. Berlin: Karger. 1921.

Throughout a long and fruitful life Professor Pick has always been interested in phenomena which illustrate the relation of mind and body. Such questions as the nature and causes of aphasia, apraxia, katatonia and hallucinations associated with lesions of the brain, have been his constant preoccupation. As one of the few writers on the Continent who have assimilated and understood the doctrines of Hughlings Jackson, he looked upon these mental changes as dissolutions of highly integrated functions and pointed out in what instances they revealed the activity of lower centres, normally kept under control. This he calls the "Neurological attitude in psycho-pathology."

The first 93 pages of his book are taken up with an essay on the value of mental medicine of the psychical changes evoked by organic nervous disease, and all the subsequent pages form examples of this method of approach. Motor and static perseveration are brought into relation with katatonia; apraxia is explained by the work of Leyton and Sherrington on the cortex, and the somewhat similar views of von Monakow are shortly discussed.

The next paper deals with the pathology of linear writing, based on a case of eclamptic psychosis. This is followed by a consideration of the exceptions to Ribot's law, that in disorders of speech the most recent acquisitions, e.g., a foreign language, are first affected. Pick then discusses the psychology of recurrent utterances in aphasia and passes on to deal with what the French have called "palilalie" or multiple repetitions. This he believes to be associated particularly with lesions of the basal ganglia.

The last paper is a description of visual hallucinations, which followed local treatment to his own eye, after the lens had been extracted for cataract. These took the form of letters projected on some surface at a distance, such as the blind, or the cheek of the person to whom he was talking. When they

appeared on a dark surface, they were surrounded by a luminous background. Such obscure phenomena already possesses a considerable and little known literature; this has been collected with the author's well-known care and thoroughness.

Der Balken. By G. MINGAZZINI. Pp. 212. Berlin : Julius Springer. 1922. M. 160.

This, the latest contribution to the series of monographs edited by Foerster and Wilmanns, is an interesting and instructive book which certainly attains the high level of the preceding volumes of the series. In successive sections the author deals with the anatomy and development of the corpus callosum, and with the symptoms which result from its destruction by vascular lesions and tumours, and from its degeneration due to other causes. Finally he discusses its function, especially from the clinical point of view, and points out the important part affections of it may play in the determination of defect phenomena in man. His general conclusion is that the corpus callosum is concerned in the eupraxia of the limbs, especially of the upper extremities, in the integration of spatial perceptions; and in the correlation of the speech mechanisms of the two hemispheres of the brain.

The author has collected together a very large amount of material and has produced a volume which cannot be neglected by the physiologist or clinician.

Functional Nervous Disorders By DONALD E. CORE. Bristol : John Wright and Sons, Ltd. Price 25s. net.

The originality of some of the views expressed in this book give it an interest to the advanced student of psychological medicine.

The classification of the functional disorders is peculiarly the author's own, and is based upon a conception of etiological factors in mental illness, particularly in hysteria, which is likely to be contested by the majority of psychologists at the present time. The functional nervous disorders are divided into regressive and progressive groups, in the former of which he places hysteria, and in the latter the sympathetic nervous disorders. He subdivides the progressive group further into what he terms the Instinct-Distortion Neuroses and the Memory Neuroses. This classification is based mainly on his conception of the term dissociation, which to him means a non-registration of memory of highly emotional incidents. The obsessional neuroses are attributed to relative inattention, dissociation not being operative in the sense in which he uses this term. He suggests that the involvement of the sympathetic nervous system in cases belonging to the progressive group induces in the course of the disease an organic disease.

He is rather scornful of psycho-analysis and concludes that it is logically inapplicable to the treatment of hysteria, though it may be used in the treatment of what he terms the obsessional form of the memory-neurosis. Few

psychotherapists of experience will agree with his opinion that the most efficient procedure in analysis is a thorough and searching cross-examination, and not free-association. An interesting chapter is devoted to a study of behaviour in man compared with the lower animals; the author arrives at the conclusion that although animals have what we term "body-memory," dependent on visceral dispositions specific to emotional tones, they can in no sense be credited with memory as we commonly understand it.

Dr. Core's views are clearly and carefully reasoned, but a careful study of this book is not likely to diminish the unfortunate confusion of opinion which obtains at the present time with regard to the etiology and treatment of the functional nervous disorders.

Archives of Neurology and Psychiatry. Edited by Sir FREDERICK MOTT. Vol. viii. London County Council. 1922.

This volume contains seventeen articles, all of which except one have been previously published elsewhere; but neurologists and psychiatrists will be grateful to the editor for having collected them together in this accessible form.

A large part of the volume is made up of studies on the pathology of dementia præcox, which are mainly from the pen of the editor. His Morison Lectures on the Psychopathology of Puberty and Adolescence, and his interesting lecture on "Body and Mind: the Origin of Dualism" are also republished here. Dr. Golla's Croonian lectures on the Objective Study of the Neuroses, and Dr. Morowoka's papers on the histology of the choroid plexus in various forms of mental disease, and the effect of exposing the brain to the gamma rays of radium, are also included.

Other interesting contributions are papers on mental defect and criminal conduct by Sir Bryan Donkin, on the neurological aspects of shock by the editor, and on chemical investigations of the cerebrospinal fluid in epilepsy, and on the metabolism in this disease by Mr. Mann.

Anormale Kinder. By L. SCHÖLZ. Third edition. Edited by A. GRÄGER. Pp. 312. Berlin: S. Karger. 1922.

The study and treatment of abnormal or defective children has been perhaps of recent years more thoroughly developed in Germany than elsewhere. In Europe, there attention has been particularly directed to the "social" training of children both at home and in special institutions under the care of adequately-equipped teachers and physicians. The system that has been thus elaborated certainly compares very favourably with our more happy-go-lucky method, which includes the provision of special schools for those who can remain at home and institutional life for the more defective whose infirmities make it impossible to allow them to mix with the rest of the family.

This book was originally prepared for teachers and officers of institutions.

for defectives, as well as for the medical students and practitioners; the additions and modifications it has received from its present editor have been developed with the same aim. It is therefore essentially a practical book. The psychology of the child, the various types of mental feebleness and deficiency, and the physical traits associated with them, are first considered. The following chapters deal with nervousness, hysteria, epilepsy and the various psychopathies, but the most striking and valuable portion of the book is that devoted to treatment, education, and training. It is written simply and directly, and can be strongly recommended to all on whom fall the duties of the care and education of the abnormal child.

Psychology.—A Study of Mental Life. By ROBERT S. WOODWORTH.
London: Methuen and Co. 1922.

This book is intended for students beginning the study of psychology, and its aim is to represent to them in simple and reasoned fashion the present state of this very active science. In this aim it succeeds exceedingly well, and it should prove a useful and stimulating textbook on the subject. It has a distinctly physiological setting, which adds to its value as a textbook.

Defining psychology as the science of behaviour, it studies first the simplest forms of behaviour as illustrated in reflexes and elementary forms of stimulus response, and then passes to the discussion of sensations, perceptions and thoughts as the reactions of higher nervous levels to stimuli of different kinds. The "stimulus response" theory is then enlarged to include motives, interests and purposes as predisposing tendencies to the production of the different reactions and responses that constitute behaviour. From this there follows naturally a division of behaviour into native and acquired reactions, and a consideration of these two classes in detail. Several chapters are devoted to the instincts and their accompanying emotions, to feeling tone and the various sensations, to attention and intelligence, until, finally, we come to the discussion of learning and habit formation, of memorizing and the laws that govern the association of mental processes of perception, reasoning, imagination and the will. Last of all there is a chapter on Personality.

The "unconscious" is dealt with adequately, and while very considerable credit is given to the originality and value of Freud's views there is some very sane and unimpassioned adverse criticism, which is not the least valuable part of the book from the beginner's point of view.

Deutsche Psychologie. By Dr. ERNST KRETSCHMER. Leipzig:
Georg Thieme. 1922.

Given to students and practitioners who have chosen the mental illnesses as their special department this little handbook will be found of great interest and value. Unlike the majority of textbooks on this subject it does not deal

with the disorders of the mind in a purely descriptive fashion, but treats them on strictly scientific lines as results of disturbances of normal psychological processes.

Acknowledging the debt that psychiatry owes to normal psychology he passes on to a consideration of mental development, paying particular attention to the part played by the emotions, and discusses the theory of ambivalence and the part it takes in complicating the affective life of the individual. The precise position of dream experience is discussed in its relation to the conscious life of the subject, and to that part of it which lies outside the immediate sphere of awareness. From this the author naturally passes on to a consideration of the state of hypnosis, and thence to hysteria and schizophrenia. The chapter on the Instincts is particularly good in that the normal and the abnormal are treated together, bringing home very forcibly the fact that in all divergences from normal behaviour the underlying processes are psychologically unchanged, but inadequate to the immediate reality at the time.

The last chapter discusses fully all the present-day technical methods of investigating mental illnesses from the psychological point of view, and the necessary therapeutic measures. He appears to be sympathetically disposed towards the Freudian technique, but does not rule out other methods.

The Poetic Mind. By FREDERICK C. PRESCOTT. New York: Macmillan and Co. 1922.

The author has applied the results of recent psychological investigations to the subject of poetic inspiration, and has produced a closely reasoned and well informed book. His outlook is primarily literary rather than psychological, psychological concepts are used to elucidate the nature of the poetic impulse without any desire to make a contribution to pure psychology. At the outset the author prepares us for his opinion that the treatment of the poet's mind must result in general conclusions, and not in the scientific formulæ of a fixed science of æsthetics. The poet's fancy springs from the vicissitudes of personal experience, expressed in dream-like form, shaped by imagination and contorted by repression, springing forth to "cleanse the bosom of that perilous stuff which weighs upon the heart."

It is certainly one of the books on psychology applied to art that repays reading; it is well written as befits a literary theme, tentative, sober and suggestive.

Ueber die Bedeutung und Entstehung der Stereotypen. By KLÄSI. Pp. 109. Berlin: S. Karger. 1922. M. 30.

Stereotypy, as defined by the author, is the autonomous manifestation of motor, speech or psychical functions reiterated over long periods in exactly the same form, and neither associated with any emotion, nor adapted to

objectively purposive end. He distinguishes two main types; those of the one group are either determined by hallucinations and can be consequently regarded as forms of defence reaction, or they may be interpreted as ceremonies or incantations for the reinforcing or symbolizing of a rite resulting from a delusion or hallucination. Stereotypies of the other group are relics of a former occupation or habit and were consequently originally purposive; these are distinguished by the fact that they can be easily modified and altered.

This monograph is a valuable study in a difficult and rather neglected region of psychopathology.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.



JAN

[OCTOBER, 1922.]

BRAIN.

PART 2, VOL. 45.

RÉFLEXES DE DÉFENSE.¹

PAR J. BABINSKI.

MESSIEURS,—J'ai entendu raconter l'anecdote suivante: le grand seigneur espagnol auquel Cervantes a dédié son livre "Don Quichotte," voyageant en France arrive à une heure tardive dans une localité où il se propose de passer la nuit. Il sonne à une auberge dont le patron, avant d'ouvrir la porte, demande à qui il a affaire. Le noble gentilhomme décline ses noms: Duque de Bejar, Marques de Gibrleon, Conde de Bañalcazar y Bañares, Visconde de la Puebla de Alcocer, Señor de las Villas de Capilla, Curiel y Burguillos. L'aubergiste, qui ignorait qu'un espagnol pouvait avoir six ou huit noms différents, réplique: Messieurs, vous êtes beaucoup trop nombreux, je ne puis vous loger; il laisse le seigneur dans la rue et se prive ainsi d'un hôte qui lui aurait valu un beau bénéfice. Une mésaventure un peu analogue est arrivée à un étudiant en médecine désireux d'apprendre la sémiologie des maladies du système nerveux. Parcourant la table des matières d'un livre qu'on lui avait recommandé, il trouve en particulier, pour ce qui concerne l'examen des membres inférieurs, l'indication des signes suivants: réflexes de défense, réflexe antagoniste de Schaefer, Unterschenkelphaenomen d'Oppenheim, reflexe fléchisseur dorso-plantaire de Bechterew, triple retrait du membre inférieur, phénomène des raccourcisseurs, réflexes d'automatisme médullaire, massreflex. Ne sachant pas que toutes ces dénominations se rapportaient, au moins en très grande partie, à un seul et même phénomène, et se jugeant incapable de loger dans son esprit tant de données qu'il croyait différentes, il renonça à cette étude et se priva ainsi d'une notion facile à acquérir et qui lui aurait été très utile.

Je ne veux pas soutenir que le sujet dont je me propose de vous entretenir soit en tous points définitivement fixé et ne comporte plus de discussion; vous verrez dans la suite qu'il n'en est pas ainsi; mais je

¹ A Lecture delivered at the Royal Society of Medicine, London, with presentation of cases and cinematograph films.

crois pouvoir dire que la question est fort simple en ce qui regarde la clinique, les moyens qu'il faut employer pour mettre en évidence les réflexes dont nous allons nous occuper et certaines conséquences que l'on peut en déduire pour le diagnostic.

Me plaçant d'abord sur le terrain de l'observation et écartant les interprétations pathogéniques, je vais décrire les phénomènes que j'ai en vue. Il s'agit de réactions motrices consécutives à des excitations cutanées ou à des excitations profondes. Pour commencer, j'envisagerai uniquement les réactions observées aux membres inférieurs du côté excité, faisant abstraction des orteils (c'est là une dissociation artificielle il est vrai, mais vous verrez ultérieurement pourquoi je la fais) et me bornant à observer les mouvements exécutés par le pied, la jambe et la cuisse. Voici en quoi consistent ces réactions : sous l'influence d'excitations du membre inférieur telles que le frottement de la plante du pied avec une épingle, le pincement de la peau de la région dorsale du pied ou de la jambe, notamment à sa partie inférieure, il se produit, outre une contraction du fascia lata, une flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin ; l'attitude en flexion se maintient généralement un laps de temps appréciable et le membre inférieur ne reprend qu'avec une certaine lenteur son attitude primitive ; dans certains cas, la contraction musculaire dure dix, quinze secondes, davantage même, surtout si l'excitation qui a provoqué le mouvement est continue, et il est possible quelquefois de déterminer ainsi une sorte de contracture transitoire.

Ce mode de réaction (triple flexion) susceptible d'être obtenue par des excitations portant sur diverses parties du membre inférieur est un des plus communs et l'on a couramment l'occasion de l'observer en clinique. On le constate ordinairement chez des malades présentant des troubles notables de la motilité volontaire, et c'est là qu'il acquiert le maximum d'intensité, mais il peut être très net chez des sujets encore assez valides.

L'électrisation avec des courants voltaïques ou avec des courants faradiques, l'application d'un corps chaud ou d'un corps froid, la pression exercée sur les parties profondes, les tractions constituent aussi des procédés d'excitation. Bechterew, puis Pierre Marie et Foix, ont recommandé une manœuvre indiquée déjà par Charcot et qui consiste à fléchir fortement les orteils sur la plante, en même temps qu'on comprime l'extrémité antérieure du pied.

La zone réflexogène est plus ou moins étendue suivant les cas. Souvent, elle occupe seulement le pied et la jambe et s'arrête au genou, mais parfois elle s'étend même à la cuisse et à une partie plus ou moins vaste du tronc ; nous reviendrons ultérieurement sur ce point.

ment sur ce point. Dans certains cas, tandis que l'excitation du pied et de la jambe donne lieu au mouvement habituel, c'est à dire à la triple flexion, une irritation portant sur la cuisse est suivie d'une extension des trois segments. Voici une autre modalité de la réaction dont je m'occupe : le pincement de la peau de la partie inférieure de la jambe est suivi d'une flexion du pied et d'une extension de la jambe sur la cuisse ; j'ai particulièrement observé cette modalité chez des malades plus ou moins contracturés, dont les jambes, qui d'habitude se maintenaient en extension, avaient été préalablement placées par moi en demi-flexion. Il m'est arrivé aussi de voir ceci : l'excitation, provoquant toujours une flexion du pied, accentuait un peu, pour commencer, l'attitude de la jambe en flexion, laquelle était immédiatement suivie d'un fort mouvement en sens inverse qui ramenait la jambe en extension. Parfois, quel que soit le sens du mouvement, flexion ou extension, on constate des contractions dans les muscles de groupes opposés, et l'on peut concevoir que le sens du mouvement soit conditionné en partie par la position où se trouvent au moment de l'excitation les segments du membre les uns par rapport aux autres.

Il y a de grandes différences en ce qui concerne l'intensité des réflexes, l'amplitude des mouvements. Tantôt, le moindre atouchement de la peau d'un membre suffira à déclencher une flexion très prononcée de tous ses segments et amènera une série de mouvements alternatifs de flexion et d'extension ; tantôt, au contraire, le pincement très vif de la peau ne déterminera qu'avec peine une simple flexion du pied. Entre ces types extrêmes se placent tous les intermédiaires. En outre, il est à remarquer que si, pour chaque malade, il existe, au cours d'un examen, une certaine proportionalité entre l'intensité de l'excitation et celle de la réaction, le rapport entre ces deux éléments peut varier notablement lorsque l'on considère les résultats de deux examens pratiqués à quelques jours ou même à quelques heures d'intervalle.

La description qui précède se rapporte à des observations faites sur des sujets atteints d'affections organiques intéressant la voie pyramidale. Mais, avant d'aller plus loin, je dois discuter les questions suivantes : les réactions signalées sont-elles toutes pathologiques ; quelques-unes d'entre elles peuvent-elles au contraire être obtenues à l'état physiologique ; y a-t-il des caractères permettant d'affirmer la nature pathologique de ces réactions ou de quelques-unes d'entre elles ?

Pour résoudre le problème, il est indispensable d'avoir examiné un grand nombre d'individus normaux et de savoir comment chez eux les membres inférieurs se comportent vis-à-vis d'excitations diverses. Or, il paraît bien établi. Une excitation de la plante du pied telle que celle exercée avec une épingle est souvent suivie, élimination faite

du mouvement des orteils sur lequel je reviendrai ultérieurement, d'une contraction du fascia lata que Brissaud a très bien décrite et d'une flexion du pied, de la jambe et de la cuisse. Ce sont là les mêmes mouvements que ceux qu'on observe à l'état pathologique. Mais chez le sujet normal la contraction est rapide, de courte durée, tandis que chez les malades dont il est question l'attitude en flexion obtenue par l'excitation plantaire se maintient généralement quelque temps et ne reprend que lentement sa position primitive, ainsi que je l'ai dit précédemment ; en outre chez ces derniers, l'amplitude du mouvement est bien plus marquée d'habitude. Ces différences sont souvent suffisantes pour établir une ligne de démarcation nette entre l'état physiologique et l'état pathologique. Toutefois, en se fondant uniquement sur ce qui vient d'être dit, des médecins encore peu expérimentés en clinique neurologique et n'ayant pas la vision précise de la forme des mouvements réflexes pathologiques seraient exposés à des erreurs ; ajoutons à cela que ces mouvements n'ont pas toujours la lenteur ci-dessus décrite.

Un autre caractère plus important et conduisant à distinguer l'état physiologique de l'état pathologique est le suivant : chez l'homme normal, l'excitation d'une région quelconque du membre, *hors de la plante du pied*, si elle peut provoquer un mouvement de flexion de la cuisse et de la jambe, ne donne jamais lieu à la flexion du pied. Je crois utile d'appuyer sur ce point. Sans doute, le retrait de la cuisse et celui de la jambe qu'on peut observer alors semblent volontaires et différent d'habitude des réactions réflexes par les caractères du mouvement, ainsi que par ce fait que la contraction spéciale du tenseur du fascia lata signalée plus haut fait défaut ; mais, je le répète, sans autres moyens distinctifs, la confusion entre l'état physiologique et l'état pathologique pourrait être malaisée à éviter. Au contraire, l'absence pour ainsi dire constante de la flexion du pied chez le sujet normal (exception faite pour un cas de simulation qu'on pourrait d'ailleurs dépister) rend simple la solution du problème. *La flexion du pied obtenue par l'excitation d'une autre région que la plante du pied permet d'affirmer qu'on a affaire à un état morbide.*

Ce signe à lui seul me paraît donc décisif ; c'est le criterium de l'état pathologique. Il va sans dire que la conviction qu'il entraîne ne peut que se fortifier lorsque ce caractère s'associe au précédent, à la lenteur de la contraction et surtout de la décontraction. Au risque de décevoir l'étudiant dont je vous parlais au début de cette Conférence, je propose une expression nouvelle : "*signe de la flexion réflexe du pied*" pour désigner les réflexes pathologiques que nous étudions. Le moyen le plus simple pour constater ce phénomène est de pincer la peau du dos du pied ou de la partie inférieure de la jambe. J'insiste auprès de mes auditeurs qui sont des débutants sur l'intérêt qu'il y a à

signe, lequel a le double mérite d'être d'une exploration très facile et d'avoir une grande valeur clinique puisqu'il décèle l'existence d'une perturbation de la voie pyramidale, que celle-ci siège dans l'encéphale ou dans la moelle. S'ils retiennent seulement cette donnée, j'aurai la satisfaction de croire qu'ils n'ont pas perdu l'heure qu'ils ont bien voulu me consacrer.

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Le retrait du membre inférieur, et notamment la flexion du pied, a manifestement des rapports assez étroits avec le signe des orteils, puisque ces deux phénomènes paraissent bien caractéristiques d'une perturbation de la voie pyramidale; ces deux réactions motrices se produisent généralement dans les mêmes conditions et suivant un mode semblable; je viens de dire que dans la triple flexion la contraction et surtout la décontraction sont lentes; or, dans mon travail sur le phénomène des orteils, en 1898, je faisais déjà remarquer que le plus souvent l'extension des orteils (réaction pathologique) est exécutée avec plus de lenteur que la flexion des orteils (réaction normale). Je suis très porté à admettre—j'y reviendrai plus loin—que la pathogénie du signe des orteils ressemble à celle de la triple flexion. Mais envisageant la question du point de vue clinique et, comme je l'ai dit dans mon travail sur les réflexes de défense publié en 1914, "mettant absolument de côté tout ce qui concerne l'interprétation physiopathologique de ces phénomènes," j'ai soutenu que les liens entre les réflexes dits de défense et le phénomène des orteils ne sont pas indissolubles, que par conséquent il y avait lieu de ne pas les fusionner complètement.

MM. Marie et Foix, tout en admettant qu'ils peuvent être dissociés et tout en reconnaissant que je n'ai pas prétendu qu'il y eût différence absolue de nature entre le signe des orteils et les réflexes cutanés de défense, déclarent être d'un avis contraire au mien. "Pour nous, au contraire," écrivent nos collègues, "le signe de Babinski appartient à l'ensemble des mouvements automatiques complexes dont le mécanisme est un mécanisme de marche."

M. Walshe, sans être d'accord avec les auteurs précédents sur le mécanisme de ces réactions motrices, ne veut établir aucune distinction entre ces deux phénomènes et il écrit que tandis que je regarde la triple flexion comme de nature défensive, je considère l' "extensor response" comme un réflexe distinct et séparé, une chose à part pour laquelle je n'offre pas d'explication et qui resterait pour moi un signe mystique et inexplicable d'affection du faisceau pyramidal. Je répondrai à cela que, si je n'ai pas cherché à expliquer le phénomène des orteils quand je l'ai

décrit, je n'ai jamais dit qu'il fût inexplicable, et je ne vois pas bien ce qu'il y a de mystique à se cantonner dans le domaine de l'observation clinique; j'aurais plutôt mérité le reproche d'être "terre à terre."

Il est incontestable, je le répète, que l'extension réflexe des orteils et la flexion réflexe du pied sont, dans la majorité des cas, associées et je serais sans doute le dernier à le nier, ayant été le premier à signaler en 1900, à propos du travail de Schaefer sur le réflexe antagoniste du pied, dont je vous entretiendrai dans un instant, que, dans l'hémiplégie organique, le pincement de la peau en diverses parties du pied et de la jambe peut provoquer à la fois ces deux réactions. Mais, encore une fois, l'une peut se produire sans l'autre. On peut observer non seulement le phénomène des orteils en l'absence du signe de la flexion réflexe du pied mais aussi la disposition inverse.

J'ai cité autrefois, à l'appui de mon opinion, une Observation anatomo-clinique relatée par Dejerine, Lévi-Valensi et Long [14, 15]: il s'agissait d'un cas de paraplégie par section complète de la moelle où il existait, en même temps que des réflexes de défense très nets, une flexion plantaire des orteils des plus franches; il est à remarquer qu'il n'y avait pas trace de réaction de dégénérescence dans les muscles de la jambe. M. Walshe récuse cette Observation à cause du passage suivant qu'on y trouve: "Les pieds sont en varus équin et les orteils en flexion. Cette déformation est aujourd'hui fixée par des rétractions fibro-musculaires." La critique de M. Walshe n'est pas sans valeur. Mais il y a tout lieu de penser que ces rétractions n'étaient pas assez marquées, au moins pendant un certain laps de temps, pour entraver l'exploration des réflexes, car M. Dejerine donne à cet égard des renseignements tellement circonstanciés qu'un doute ne peut guère subsister. Il écrit en effet: "J'arrive maintenant à une question encore plus importante peut-être que les précédentes, à savoir l'état du *réflexe cutané plantaire*. Pendant les six mois que passa ce malade dans mon service, le réflexe cutané de la plante du pied se faisait des deux côtés en flexion plantaire, c'est à dire comme à l'état physiologique."

Je rappelle aussi l'observation publiée par Pastine [27] se rapportant à un sujet atteint de paraplégie motrice absolue avec troubles très accentués de la sensibilité superficielle et profonde des membres inférieurs. J'extrais de ce travail le passage suivant: "Le fait intéressant pour la question qui nous occupe me semble être celui-ci: la possibilité presque constante d'obtenir, par une excitation plantaire un peu forte ou répétée, ou encore mieux par un pincement énergique de la peau du dos des pieds, le mouvement réflexe de flexion du pied, de la jambe et de la cuisse associé à la flexion nette de tous les orteils, et par une excitation minimale du bord plantaire externe, le signe de Babinski nettement

positif et isolé Dans ce cas, c'est la flexion du gros orteil qui fait partie du mouvement général de retrait, et pourtant l'extension pathologique du même orteil existe dans toute sa pureté."

Du reste, déjà dans un travail publié par moi en mars 1899 [2], basé en particulier sur une observation qui est un type de paraplégie en flexion, avec mouvements spasmodiques intermittents accentuant la flexion des cuisses et des jambes, il est dit expressément que le réflexe cutané plantaire est normal.

Des expériences de M. Ozorio de Almeida, confirmées par moi, ont montré que chez des sujets présentant le signe des orteils, une compression du membre inférieur avec une bande élastique peut amener transitoirement la réapparition du mouvement réflexe de flexion des orteils. or, le pied peut continuer alors à exécuter un mouvement réflexe en flexion à la suite de l'excitation de sa région dorsale.

MM. Marie et Foix, dans un article sur "les réflexes d'automatisme médullaire [22]," écrivent à ce sujet: "Nous avons, sur la plupart de ces points, pu reproduire les expériences de Babinski, mais l'interprétation que nous inclinons à donner nous apparaît comme très différente de la sienne" "Il est aisé de se convaincre par l'observation attentive que l'application de la bande d'Esmarch agit en supprimant momentanément l'excitabilité réflexe des muscles ischémisés " Les muscles extenseurs, par suite des dispositions anatomiques, subiraient une ischémie plus intense que les fléchisseurs.

L'interprétation donnée par mes collègues me semble discutable Elle ne permet guère de comprendre ce fait noté chez certains sujets et que je rappelle: avant la compression, réflexe plantaire toujours en extension quelle que soit la région de la plante que l'on excite; après la compression, réflexe en extension ou en flexion suivant qu'on excite le bord externe ou le bord interne de la plante.

De plus, en variant la durée de la compression, j'ai fait plusieurs fois les constatations suivantes: après avoir enlevé la bande à un moment où le réflexe se faisait encore en extension, j'ai vu cependant, au bout de quelques instants, au retour de l'irrigation sanguine, le réflexe en flexion remplacer pour quelque temps le mouvement réflexe précédent. Il m'est arrivé alors d'observer, après avoir pincé la peau de la jambe ou du dos du pied, la flexion des orteils associée à une forte flexion du pied.

Ces faits ne sont guère en concordance avec l'interprétation proposée par MM. Marie et Foix. D'ailleurs, celle-ci serait-elle juste, elle n'infirmerait pas ma thèse, car me plaçant simplement sur le terrain de l'observation, et sans contester aucunement les relations qui unissent la flexion réflexe du pied avec l'extension des orteils, les connaissant

même depuis plus de vingt ans, comme je viens de le dire, j'ai voulu établir qu'il pouvait y avoir dissociation de ces deux phénomènes. Les cas où cette dissociation existe, sans être très communs, ne sont pas tout à fait exceptionnels; j'en ai observé déjà un assez grand nombre et vous aurez l'occasion de la constater vous-mêmes sur l'un des films que je ferai passer devant vos yeux. Il s'agit d'un malade atteint de paraplégie incomplète liée vraisemblablement à une plaque de sclérose; d'un côté on observe la trépidation épileptoïde du pied et le triple retrait associé à l'extension du gros orteil; de l'autre côté la trépidation épileptoïde et le triple retrait existent nettement, mais ce dernier phénomène coïncide avec un réflexe plantaire en flexion bien qu'il n'existe pas de réaction de dégénérescence dans les muscles de la jambe.

Avant de terminer ce chapitre, je ferai remarquer que Marie et Foix, malgré leur désaccord apparent avec moi, semblent avoir dans le fond une opinion analogue à la mienne, puisque dans leur premier article sur le retrait réflexe du membre inférieur [21] ils écrivent ceci: " Il (le retrait réflexe) est extrêmement fréquent dans l'hémiplégie constituée. Il est en général associé au signe de Babinski, mais ne lui est pas superposable. On l'observe en effet en dehors de ce signe, particulièrement chez certains pseudo-bulbaires, ou dans certains cas d'hémiplégie ancienne"; et, dans un deuxième travail sur les réflexes d'automatisme médullaire [22], ils écrivent encore: " L'on peut cependant voir, dans les cas où, par suite du combat entre le réflexe normal en flexion et le réflexe pathologique en extension, le mouvement des orteils est nul ou même en flexion, le signe des raccourcisseurs établir une lésion que la recherche du signe de Babinski n'avait pu dépister."

N'est-ce pas absolument conforme à ce que j'ai soutenu?

Il me semble intéressant, à l'appui de ma thèse, de noter que M. Van Woerkom, dans un travail " Sur la signification physiologique des réflexes cutanés des membres inférieurs " [33], écrit ceci: " Pourtant, le lien qui relie le signe de Babinski au ' flexion réflexe ' n'est pas indissoluble."*

* * * * *

Contrairement à l'usage suivant lequel l'exposé d'une question est généralement précédé de l'indication des noms de ceux qui s'en sont principalement occupés, j'ai cherché d'abord à faire une description des faits cliniques suffisante pour bien délimiter mon sujet. Je crois le moment venu de faire un historique, surtout étant donné que j'ai déjà été entraîné à signaler quelques controverses entre neurologistes.

Les phénomènes que nous étudions paraissent avoir été mentionnés

pour la première fois en 1784 par Prochaska. L'expérience faite par cet auteur a été maintes fois reproduite depuis; Schiff, Vulpian, Brown-Séquard, pour ne citer que quelques-uns des physiologistes qui se sont occupés des réflexes de défense, ont vu comme Prochaska qu'une grenouille ou un mammifère dont on sectionne la moelle dorsale retire brusquement la patte en fléchissant les divers segments de ce membre les uns sur les autres quand on en pique l'extrémité.

Ce mouvement reproduit assez exactement celui qu'effectue, sous la même excitation, une grenouille dont la moelle est intacte et qui cherche à se dérober à l'injure extérieure, à se défendre. Le phénomène fut pour cela qualifié de "mouvement réflexe de défense," et l'usage a consacré cette dénomination.

Les physiologistes seuls s'occupèrent d'abord de ces mouvements particuliers. Vulpian, Brown-Séquard signalent il est vrai leur existence dans les tumeurs de la moelle et dans quelques autres affections de cette partie du névraxe, mais ils n'en indiquent pas la valeur sémiologique précise.

L'attention qu'on leur avait prêtée fut même bientôt très réduite lorsqu'on acquit la connaissance des réflexes tendineux et qu'on s'attacha à leur étude. La brièveté des mentions qu'on trouve au sujet des réflexes de défense dans les meilleurs traités classiques de neurologie fait foi, d'ailleurs, de ce réel discrédit.

C'est depuis vingt-cinq ans environ, et à la suite de ma communication sur le réflexe cutané plantaire et le phénomène des orteils, que l'attention a été de nouveau dirigée sur les réflexes de défense, bien qu'on se soit servi parfois d'autres termes pour désigner les faits qui s'y rapportaient.

Schaefer, dans un travail publié en novembre 1899 [31], décrit un phénomène réflexe dont voici les caractères: lorsqu'on presse énergiquement, entre le pouce et l'index, le tendon d'Achille dans son tiers moyen ou son tiers supérieur, on provoque chez l'individu sain une sensation de douleur légère et en même temps une très faible extension du pied et parfois aussi une flexion des orteils. Or, dans certains cas pathologiques, chez des malades atteints d'hémiplégie cérébrale organique, la même manœuvre donne lieu à une sensation de douleur plus intense et, en outre, à une flexion du pied ainsi qu'à une extension des orteils du côté paralysé. Ce réflexe pathologique se distinguerait des autres réflexes tendineux parce que la réaction, au lieu de s'opérer dans le muscle dont le tendon est excité, se manifesterait dans les antagonistes, d'où la dénomination de *réflexe antagoniste* que Schaefer propose de donner à ce phénomène.

Ainsi que je l'ai dit dans une communication à la Société de Neurologie

en janvier 1900, il est aisé de vérifier les faits décrits par Schaefer qui sont absolument exacts, mais ses déductions comportent des critiques : d'une part, l'extension des orteils qu'il indique n'est autre chose que le phénomène des orteils découvert antérieurement ; d'autre part, rien n'autorise à admettre que la réaction obtenue dans les expériences de Schaefer constitue un réflexe tendineux antagoniste. J'ai montré, en effet, que chez les hémiplégiques qui présentent ces réactions, extension des orteils et flexion du pied, celles-ci sont généralement obtenues par le pincement de la peau seule dans le voisinage du tendon ou encore en d'autres parties du membre inférieur. Comme on le voit, ces observations ont conduit à cette notion nouvelle, dont j'ai fait ressortir précédemment l'intérêt, qu'une excitation du membre inférieur, hors de la zone plantaire, incapable de produire une flexion réflexe du pied à l'état normal, peut en déterminer une dans l'hémiplegie organique, affection dans laquelle la voie pyramidale est intéressée.

Les réactions décrites ultérieurement par Oppenheim sous la dénomination d' " Unterschenkelphaenomen " dans les affections pyramidales sont identiques aux précédentes. Voici en quoi elles consistent : tandis que l'excitation des téguments de la partie interne de la jambe provoquée par le frottement ne détermine à l'état normal aucun réflexe, ou seulement une flexion des quatre petits orteils, cette excitation, dans les cas où il y a une lésion de la voie pyramidale, produit une contraction des muscles extenseur propre du gros orteil, jambier antérieur, extenseur commun des orteils et parfois des muscles péroniers.

Van Gehuchten [32], en août 1900, dans une étude " sur les réflexes cutanés et les réflexes tendineux, " s'occupe particulièrement des réflexes de défense dans les lésions atteignant le système pyramidal, il se sert de ces termes : " mouvement de retrait brusque de tout le membre : flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin, avec mouvements d'adduction de la cuisse. "

Je reviens sur ce sujet dans un travail publié en 1904 à la Société de Neurologie et intitulé : " Sur la transformation du régime des réflexes cutanés dans les affections du système pyramidal. "

Bechterew [11] en 1906 a publié une note sur les mouvements réflexes produits par la manœuvre qui consiste à flechir le pied et les orteils.

En mai 1910, nous cherchons, Jarkowski et moi [7], à utiliser les réflexes de défense pour déterminer le niveau inférieur d'une lésion spinale.

En juillet 1910, Pierre Marie et Foix publient leur premier travail sur ce sujet [21]. Il est intitulé : " Sur le retrait du membre inférieur provoqué par la flexion forcée des orteils. "

En 1910 Claude [13] traite de l'hyperkinésie réflexe qu'on peut observer au membre supérieur.

En janvier 1911 [3], je décris "la paraplégie spasmodique avec contracture en flexion et contractions musculaires involontaires" et je fais ressortir les liens qui l'unissent aux réflexes de défense. En mai 1912, je reviens sur ce sujet [4].

Nouveau travail de Marie et Foix en mai 1912 [22], intitulé. "Les réflexes d'automatisme médullaire et le phénomène des raccourcisseurs. Leur valeur sémiologique. Leur signification physiologique."

En 1912, mémoire de van Woerkom [33]. "Sur la signification physiologique des réflexes cutanés des membres inférieurs."

En 1914-1915 [6], je publie une étude sur les réflexes de défense, et quelques semaines plus tard Pierre Marie et Foix [23] font paraître à leur tour un mémoire sur "les réflexes d'automatisme médullaire dits de défense."

Dans un travail intitulé. "Quelques remarques sur les réflexes de défense dits d'automatisme médullaire" [18], Jarkowski discute la pathogénie de ces phénomènes.

Voici maintenant l'indication de plusieurs travaux sur le sujet qui nous occupe qui sont l'œuvre de neurologistes anglais :

F. M. R. Walshe: "The Physiological Significance of the Reflex Phenomena in Spastic Paralysis of the Lower Limbs" [34], et "On the Genesis and Physiological Significance of Spasticity and other Disorders of Motor Innervation" [35].

Henry Head and George Riddoch: "The Automatic Bladder, Excessive Sweating and some other Reflex Conditions in Gross Injuries of the Spinal Cord" [17].

George Riddoch: "The Reflex Functions of the Completely Divided Spinal Cord in Man" [28], et "The Clinical Picture of Complete Transverse Division of the Spinal Cord" [29].

George Riddoch and Farquhar Buzzard: "Reflex Movements and Postural Reactions in Quadriplegia and Hemiplegia, with especial reference to those of the Upper Limb" [30].

Je fais une place à part au grand physiologiste Sherrington dont les découvertes ont orienté les recherches des neurologistes anglais et les ont inspirés dans leurs interprétations des faits cliniques observés. Le nom de Philipson, collaborateur de Sherrington, mérite aussi d'être particulièrement retenu.

Après ce court historique, reprenons le fil de nos idées. J'ai dit que si le lien entre les réflexes de défense pathologiques, notamment la flexion

réflexe du pied et le signe des orteils, n'est pas indissoluble, il est pourtant assez étroit.

Et quelles sont les relations entre ces diverses réactions et la surréflexivité tendineuse qui elle aussi constitue un signe de perturbation de la voie pyramidale ? On peut dire, *a priori*, que ces deux ordres de phénomènes doivent être souvent associés, mais c'est une liaison beaucoup moindre que la précédente. Dans le *tabes dorsalis* spasmodique avec surréflexivité tendineuse extrêmement forte, la flexion réflexe du pied est généralement faible ou même fait défaut, ce qui, à la vérité, pourrait tenir à la contracture en extension qui entrave la manifestation des réflexes de défense. Dans l'hémiplégie organique avec exagération notable des réflexes tendineux et trépidation épileptoïde, la flexion réflexe du pied peut aussi manquer de même qu'il y a parfois absence du signe des orteils.

Mais ce qui est plus frappant c'est la disposition inverse. affaiblissement ou abolition des réflexes tendineux avec exagération notable des réflexes de défense. C'est ce qu'on observe d'habitude dans la maladie de Friedreich ; c'est ce qu'on peut voir dans le *tabes* associé à une lésion pyramidale. J'ai insisté déjà en 1898, dans un travail relatif au phénomène des orteils [1], sur la coexistence de ce signe avec la subréflexivité ou l'irréflexivité tendineuse. "J'ai constaté, disais-je, ce phénomène dans plusieurs cas d'hémiplégie récente flasque, où les réflexes tendineux étaient normaux, affaiblis ou même abolis du côté paralysé."

On observe très couramment des malades atteints de paraplégie crurale plus ou moins marquée avec réflexes tendineux normaux, sans trace de trépidation épileptoïde du pied et avec réflexes de défense très caractérisés. Je suis convaincu, certain même, qu'autrefois beaucoup de malades de ce genre ont été considérés comme atteints de paraplégie hystérique. Ces erreurs sont devenues bien plus rares depuis que la connaissance des signes en question s'est répandue parmi les praticiens.

Dans la paraplégie en flexion, sur laquelle je reviendrai plus loin et dont le trait le plus essentiel est l'exagération des réflexes de défense, les réflexes tendineux peuvent aussi être exagérés, mais il n'en est pas toujours ainsi : ils sont parfois d'une intensité moyenne, ils peuvent être faibles et semblent même abolis dans certains cas. Je sais bien que l'exploration des réflexes tendineux est rendue quelquefois difficile par les rétractions fibro-tendineuses, par l'intensité et la fréquence des spasmes qui se produisent ; mais en renouvelant les explorations à plusieurs reprises, en saisissant, pour les pratiquer, les moments où le spasme cesse, il est ordinairement possible de se rendre compte de l'état de la réflexivité tendineuse. Si j'ai bien compris ce qu'a écrit M. Walshe

à ce sujet, il est d'avis que dans la paraplégie en flexion, si les réflexes tendineux des extenseurs peuvent être abolis, ceux des fléchisseurs sont toujours exagérés. Je ne puis souscrire à cette opinion, m'étant assuré dans quelques cas de paraplégie en flexion que les réflexes tendineux des fléchisseurs de la jambe sur la cuisse n'étaient pas du tout au-dessus de la normale et paraissaient même plutôt faibles.

Dans la paraplégie en flexion, l'affaiblissement des réflexes tendineux peut survenir après une période plus ou moins longue pendant laquelle il y a eu surréflexivité tendineuse. Mais il y a des cas où, dès le début, les réflexes tendineux sont amoindris. J'ai rapporté une Observation de ce genre; voici un passage du travail où ce fait est relaté [4] : "Ce qui est capital c'est que, chez cette malade, où l'existence d'une affection organique de la moelle intéressant les faisceaux pyramidaux est incontestable, on observe une contracture associée à une abolition à peu près complète des réflexes tendineux et à des réflexes de défense extrêmement forts. Ce fait constitue un nouveau document relatif à l'histoire de la *paraplégie spasmodique organique avec contracture en flexion et contractions musculaires involontaires*, et il mérite pour plusieurs motifs d'attirer l'attention.

"Tandis que, chez les sujets où la contracture en flexion est permanente et a acquis une grande intensité, la faiblesse ou l'abolition des réflexes tendineux est difficile à apprécier et ne peut être affirmée qu'après des examens plusieurs fois renouvelés; dans le cas particulier, la contracture en flexion étant intermittente, on est à même, pendant les phases de détente qui sont très fréquentes, de se rendre un compte exact des réflexes tendineux; on s'assure aisément que le réflexe rotulien droit et les réflexes achilléens sont abolis. J'ajoute que l'affaiblissement des réflexes tendineux a été noté, dans ce cas, dès le début de l'affection et n'a pas été précédé de l'exagération de ces réflexes, ainsi que cela se voit assez souvent dans cette forme de paraplégie."

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L'exagération des réflexes de défense conduit-elle seulement au diagnostic de perturbation de la voie pyramidale? N'est-elle pas en mesure de fournir d'autres renseignements ayant une portée pratique, notamment dans les cas de compression de la moelle? C'est une question que nous avons cherché à résoudre, Jarkowski et moi. Mais il est de mon devoir de signaler un passage relatif à ce sujet que j'extraits de l'ouvrage de Duchenne de Boulogne "De l'électrisation localisée" et qui nous avait échappé autrefois: "Le point où le chatouillement de la peau cesse de provoquer des contractions réflexes indique

le niveau où existe la compression de la moelle." Il est à noter que ce moyen de localisation n'avait jamais été utilisé jusqu'à nous par aucun des neurologistes qui s'étaient occupés de repérer les tumeurs comprimant la moelle en vue de l'intervention chirurgicale. Voici, en résumé, ce que nous avons cru pouvoir déduire de nos investigations. Dans tout le territoire cutané en rapport avec la portion de la moelle sous-jacente à la partie inférieure de la lésion et dans ce territoire seulement, du moins quand la paraplégie est très marquée, une excitation peut provoquer des réflexes de défense. On possède ainsi un moyen de déterminer la limite inférieure de la compression. Ce n'est pas là une vue théorique. Cette donnée est établie déjà sur un certain nombre d'observations où le diagnostic a été vérifié pendant l'opération.

On a aussi publié, il est vrai, quelques faits qui tendent à infirmer cette notion, mais la contradiction n'est peut-être qu'apparente et j'ai cherché à l'expliquer dans mon travail de 1914, dont j'extrais le passage suivant :

"Cela tient, je pense, aux difficultés nombreuses que l'on rencontre quand on s'efforce de délimiter le territoire des réflexes de défense. On est exposé à des erreurs d'observation et d'interprétation sur lesquelles je crois devoir insister.

"C'est ainsi que chez des malades ayant conservé en partie leur motilité volitionnelle, un mouvement volontaire pourrait faire prendre le change et être considéré à tort pour un réflexe de défense. Chez d'autres malades, un mouvement spasmodique 'spontané' risque d'être attribué à une excitation provoquée par l'expérimentateur, s'il coïncide avec cette dernière. On saisit immédiatement la portée d'une telle confusion, si cette excitation a été appliquée au-dessus du territoire de réflexes de défense.

"D'autre part, la réflectivité peut varier au cours d'un même examen et, a fortiori, d'un jour à l'autre ; on obtient ainsi des résultats en apparence contradictoires. De plus, la surréflectivité, que nous avons en vue, n'atteint son niveau maximum qu'à une période plus ou moins tardive de l'évolution de la maladie.

"Il faut donc renouveler les explorations pendant plusieurs jours, au besoin pendant plusieurs semaines, et retenir, entre les limites variées qui ont été obtenues, celle qui est la plus élevée, qu'elle se trouve des deux côtés au même niveau ou à des hauteurs différentes, pourvu qu'elle soit dûment établie.

"Il est encore essentiel de savoir que les réflexes de défense se laissent provoquer beaucoup plus facilement sur les membres inférieurs que sur le tronc et que parfois le domaine de la surréflectivité ne dépasse pas le pli de l'aîne, même lorsque la limite inférieure de la lésion siège à la

partie moyenne de la moelle dorsale ou au-dessus. Notre expérience nous a appris qu'il fallait seulement tenir compte des cas où la surréflexivité envahit une partie plus ou moins étendue du tronc, à moins que d'autres symptômes ne permettent déjà de localiser la lésion dans la région lombaire ou sacrée.

"Enfin, je rappelle que les réflexes de défense se laissent provoquer de préférence tantôt par le pincement, tantôt par le froid, la chaleur, l'électricité ou la piqure. Dans chaque cas particulier, il faut employer le mode d'excitation qui constitue le réactif le plus sensible.

"On voit, par ce qui précède, combien ces recherches sont délicates, et je conviens qu'un observateur, quelque averti et méthodique qu'il soit, ne parviendra pas toujours à obtenir de ses investigations sur les réflexes de défense des renseignements utilisables."

Il n'en est pas moins vrai, pensons-nous, que dans certains cas de compression spinale il sera possible d'acquérir ainsi des données intéressantes pour le diagnostic topographique des lésions, surtout si on les rapproche de celles, plus importantes sans aucun doute, qui sont fournies par les troubles de la sensibilité

Autre problème. L'intensité des réflexes de défense et les diversités de forme qu'ils présentent sont-elles en rapport avec l'intensité des lésions, le niveau où elles siègent et leur nature? Dans mon article de 1898 j'écrivais déjà ceci à propos du signe des orteils: "Il faut donc bien remarquer que ce signe, s'il révèle l'existence d'une perturbation dans le système pyramidal, n'en dénote pas la gravité. . . . Il semble même qu'il puisse parfois constituer le seul indice de cette perturbation." Je reviendrai dans un instant sur ce point.

Pour ce qui est relatif au niveau, j'ai dit autrefois et tous les neurologistes semblent d'accord là-dessus, que les réflexes de défense sont, d'une manière générale et sauf à la période initiale quand il y a shock, plus accentués dans les lésions spinales que dans les lésions cérébrales, ce qui tient peut-être en partie à ce que d'ordinaire les premières sont bilatérales, les secondes unilatérales.

En ce qui regarde la nature des lésions, d'après ce que j'ai observé, je pense que l'exagération des réflexes de défense est particulièrement intense et durable dans les cas de paraplégie spasmodique par compression de la moelle ou par sclérose spinale dans lesquels les altérations dégénératives du faisceau pyramidal font défaut ou sont peu prononcées. Plusieurs observations tendant à confirmer cette opinion ont été rapportées par divers auteurs [26].

Les faits de section complète de la moelle observés à la suite de traumatismes de guerre ont montré à MM. Head, Riddoch, à M. Lhermitte que ces lésions, qui produisent le maximum de dégénération peuvent aussi se manifester, à une certaine période de leur évolution, par des réflexes de défense très marqués. Mais dans ces derniers cas, la phase pendant laquelle les réflexes de défense sont exagérés est relativement courte et la contracture qui se lie à ces réflexes dans la paraplégie que j'ai envisagée et dont nous aurons à nous occuper dans la suite, manque ou est peu marquée. En tout cas, mes observations ont montré que l'intensité des réflexes de défense n'est pas, tant s'en faut, en proportion directe avec le degré d'intensité de la dégénération secondaire. M. Walshe, à ce propos, dit ceci : Le point soulevé par Babinski qu'il peut n'y avoir que peu ou pas de dégénération secondaire de la voie pyramidale à l'examen anatomique dans de tels cas n'a pas de signification spéciale parceque, comme Gordon Holmes l'a montré, il n'y a pas de relation directe, constante entre la gravité des manifestations cliniques et la dégénération descendante secondaire. Une lésion en foyer de la moelle, dit-il, peut causer une paralysie spastique extrême et perte du contrôle sphinctérien, et cependant, à l'autopsie, il peut ne pas y avoir de dégénération spinale descendante.

Je sais cela depuis longtemps et j'ai précisément rapporté moi-même en 1899 une Observation de ce genre que j'ai déjà rappelée. Mais il faut savoir aussi qu'une paralysie complète due à une compression de la moelle, accompagnée de réflexes de défense très intenses, peut guérir totalement ; et cette régression des accidents n'est elle pas explicable par l'absence de dégénération ? C'est ce que j'ai cherché à mettre en lumière.

Je le répète, la présence de réflexes de défense même très prononcés et avec accompagnement de troubles moteurs des plus marqués, n'est pas nécessairement l'expression d'un état incurable. Entre autres faits à l'appui de cette notion, je puis vous citer quelques extraits d'une Observation publiée par Jarkowski, Lecène et moi [10] et intitulée : "Paraplégie crurale par néoplasme extra-dure-mérien. Opération. Guérison." En décembre 1911, on note ceci : "La malade présente une paraplégie spasmodique en extension avec troubles de la sensibilité remontant jusqu'à la ligne mamelonnaire. La paralysie des membres inférieurs est complète et ne cède même pas sous l'influence de divers procédés dynamogénisants (faradisation, application de la bande d'Esmarch). Cette contracture ne peut être vaincue que par un très grand effort ; pourtant, elle n'est pas toujours égale à elle-même et peut être diminuée par des mouvements passifs. De plus, la contracture en extension est entrecoupée de temps à autre par des mouvements spasmodiques invo-

lontaines qui déplacent brusquement les membres inférieurs, fléchissent la cuisse, la jambe et le pied, les allongent ensuite avec une grande force, en détachant le membre du plan du lit, et ainsi de suite, jusqu'à ce que le membre retrouve sa position primitive de repos.

" Ces spasmes se produisent soit dans un seul des membres inférieurs, soit dans les deux, et alors tantôt ils revêtent la même forme des deux côtés, tantôt ils donnent lieu à une flexion à droite et une extension à gauche ou vice-versa. Les réflexes tendineux des membres inférieurs sont nettement exagérés ; il y a de la trépidation épileptoïde du pied des deux côtés.

" On constate le signe des orteils des deux côtés.

" Les réflexes de défense sont fortement exagérés et peuvent être provoqués même par des excitations très légères. Leur forme varie suivant la position des membres et l'endroit de l'excitation, mais elle est sensiblement pareille à celle des spasmes involontaires spontanés."

La malade est opérée en janvier, 1912. L'intervention est suivie d'une amélioration qui se poursuit ensuite, mais lentement.

En juin 1914, on note : " Elle marche toute seule, sans canne, pas très vite, il est vrai, mais d'une manière à peu près normale ; elle ne traîne pas ses jambes ; elle ne fauche pas ; la pointe du pied ne butte pas contre le sol.

" Un examen objectif minutieux ne décèle comme reliquat des troubles d'autrefois qu'une tendance à l'extension des orteils et une légère exagération des réflexes de défense."

J'apprends ultérieurement que la guérison est devenue complète.

Ce n'est pas dans la patrie de l'illustre Horsley dont je m'honore d'avoir été l'ami, que je provoquerai de la surprise en rapportant l'observation d'une paraplégie due à une tumeur comprimant la moelle et guérie à la suite d'une intervention chirurgicale. Si je l'ai relatée, c'est afin de bien mettre en évidence ce fait que la surréflexivité défensive n'implique pas l'idée d'incurabilité.

Les réflexes de défense, après disparition complète des troubles moteurs, peuvent redevenir absolument normaux.

On a pris l'habitude de dire que l'exagération des réflexes de défense témoigne que la moelle est délivrée du joug des centres supérieurs ; mais, comme on le voit par ce qui précède, la moelle, en recouvrant les réflexes de défense de ses ancêtres, n'a pas reconquis toute leur indépendance. pareille aux affranchis de Rome, elle ne jouit parfois que d'une liberté transitoire et elle est exposée à reprendre ses chaînes, ce qu'atteste le retour des réflexes à l'état physiologique.

Mais il y a plus dans certains cas, les réflexes de défense pathologiques survivent à tous les autres troubles.

Entre autre malades de ce genre, j'en puis citer un qui, guéri d'une paraplégie par lésion syphilitique de la moelle, avait recouvré la motilité au point de pouvoir parcourir sans arrêt une distance de plus de dix kilomètres et qui cependant présentait d'une manière très nette le signe des orteils et le signe de la flexion réflexe du pied.

On peut dire qu'en pareille occurrence il s'agit de la part de la moelle d'une fanfaronnade, d'un bluff. elle affiche des airs d'indépendance, se prétend libérée, tout en obéissant servilement à l'encéphale, son maître.

Si la diminution progressive des réflexes de défense préalablement exagérés peut être un signe favorable, comme dans l'observation de tumeur que je viens de rapporter, elle peut au contraire dénoter une aggravation : dans les cas de section complète de la moelle, ces réflexes s'affaiblissent d'habitude à la période qui précède la mort.

J'ai été amené à vous indiquer l'état des réflexes de défense dans les sections spinales totales à la phase terminale, à la phase moyenne. Je dois vous exposer l'état de ces réflexes à la première phase, après le traumatisme. Sous l'influence du shock, les réflexes cutanés aux membres inférieurs peuvent être complètement abolis comme le sont les réflexes tendineux. Pour ce qui concerne les réflexes tendineux, dont je ne vous parle qu'incidemment, et contrairement à l'opinion émise par Bastian et acceptée pendant trente ans par la majorité des neurologistes, leur abolition n'est pas non plus définitive ; ils peuvent reparaitre et même atteindre un degré plus élevé que la normale, mais leur retour est plus tardif que celui des réflexes cutanés. Au sujet de ces derniers, les opinions ne sont pas toutes concordantes, ce qui tient sans doute à la diversité des cas et à ce qu'un même auteur a eu seulement l'occasion d'observer un nombre de faits restreint. Il y aurait tantôt abolition du réflexe cutané plantaire, tantôt extension, tantôt flexion des orteils. D'après Guillain et Barré, le réflexe en flexion de ces paraplégiques se différencie de celui de l'homme sain par sa lenteur, son temps de latence prolongé, la persistance relative de l'attitude en flexion. Dans cette première phase, la zone réflexogène serait limitée, comme à l'état physiologique, à la zone plantaire, et ce n'est qu'ultérieurement qu'elle s'étendrait à tout le pied et à la jambe ; les réflexes deviennent de plus en plus forts et une exagération parfois très marquée des réflexes de défense se constitue alors.

Il y a lieu de comparer ces faits de paraplégie à début brusque avec les cas d'hémiplégie cérébrale succédant à un ictus apoplectique. Souvent, dès les premiers jours, alors que le malade est encore dans le coma, que la paralysie est complète et la surréflexivité tendineuse d'habitude affaiblie, on peut constater l'extension réflexe des orteils et la flexion.

qu'il n'en est pas toujours ainsi. A la page 63, où il est fait mention de l'état des reflexes cinquante-deux jours après l'examen précédent, nous trouvons ceci : "Les mouvements de défense sont toujours très accusés. Le pincement de la peau de la face antérieure de la cuisse détermine l'extension de la jambe et la contraction tonique du quadriceps ; quelquefois, le mouvement s'étend au membre opposé."

(c) Présence de ce que les auteurs anglais appellent "local sign" et qui consiste en ce que les réactions seraient différentes suivant les points excités. Si, par exemple, l'excitation de la plante du pied, selon qu'elle porte sur sa partie externe ou sa partie interne, provoque, outre la triple flexion, une abduction ou une adduction du pied, on pourrait affirmer que la section est incomplète.

D'après Riddoch, si je l'ai bien compris, dans la section incomplète, la zone réflexogène du réflexe en flexion ne dépasserait pas le genou. Cette opinion me semble en contradiction avec certains faits. Vous verrez sur un des films une malade atteinte de paraplégie incomplète ; elle peut mouvoir volontairement ses membres inférieurs et cependant l'excitation de l'abdomen avec un tube de glace provoque une flexion comme l'excitation du pied.

Par contre, on pourrait considérer, d'après MM. Head et Riddoch, comme caractéristique d'une *section totale*, d'une libération complète de la moelle, ce qu'ils appellent "Massreflex," c'est à dire réflexes, de défense toujours en flexion avec mictions réflexes et forte sudation dans le segment inférieur du corps.

J'ai eu l'occasion de décrire moi-même les troubles vésicaux en question dans mon travail déjà cité. Voici le passage qui s'y rapporte :

"Les grands mouvements des membres, qui s'imposent surtout à l'attention, furent seuls étudiés au début, mais un examen minutieux montre que d'autres groupes musculaires peuvent entrer en jeu, comme cela résulte des recherches faites par mon élève Barré. La contraction des muscles de la paroi abdominale provoque un retrait de l'abdomen ; celles des muscles de la paroi thoracique produit des spasmes respiratoires brusques. Ces divers mouvements se font généralement en même temps que ceux des membres ou les suivent à très court intervalle. Enfin, les muscles profonds du tronc, ceux qui sont en partie volontaires, comme le diaphragme, ou ceux qui sont spécialement adaptés à la vie végétative, comme les muscles intestinaux et les muscles vésicaux, peuvent également entrer en contraction en même temps que les muscles des membres ; les malades ont parfois alors des débâcles gazeuses ou des mictions involontaires qui témoignent de la mise en activité de certains de leurs muscles lisses."

Y a-t-il là des éléments de différenciation ?

Ce que je puis dire c'est que nous avons suivi très longtemps, Jarkowski et moi, un sujet atteint d'une paraplégie liée à des lésions spécifiques, paraplégie très grave, mais dans laquelle les mouvements volontaires n'étaient pas complètement abolis ; la moelle n'était donc pas entièrement libérée des centres supérieurs ; or, chez ce malade, bien souvent, des excitations diverses déterminaient, en même temps que des réflexes de défense, des mictions involontaires et l'évacuation de matières fécales.

Avant de terminer ce chapitre je ferai remarquer que l'on a très rarement l'occasion d'observer des cas avérés de section totale. Ce sont les blessures de guerre qui ont fourni le matériel d'études. Sans elle, la prétendue loi de Bastian ne serait pas encore abrogée. Mais avouez que les acquisitions neurologiques nouvelles sont une bien faible compensation des misères déchainées par la catastrophe mondiale.

* * * *

Quelques mots sur les mouvements réflexes des membres supérieurs.

Claude, dans un travail : " Sur certains phénomènes d'hyperkinésie réflexe " [13] a décrit dans l'hémiplégie cérébrale des réactions motrices réflexes et a eu surtout en vue celles du membre supérieur.

J'ai mentionné des réflexes de défense du membre supérieur dans mon article de 1915 : " Ils consistent également, disais-je, en mouvements de retrait ou d'allongement, souvent combinés à de la pronation de l'avant-bras et de l'adduction du bras. Ces mouvements peuvent présenter des modalités diverses comme les réflexes du membre inférieur, mais ils sont plus souvent que ceux-ci localisés à un seul côté."

MM. George Riddoch et Farquhar Buzzard [30] ont fait une étude approfondie de ces réactions motrices dans un travail dont j'ai donné déjà l'indication bibliographique et sur lequel le manque de temps m'empêche d'insister.

* * * *

Comment se comportent les réflexes de défense pendant le sommeil artificiel ? Cela dépend sans doute de l'agent anesthésiant dont on fait usage. On sait que l'éther agit autrement sur les réflexes tendineux que le chloroforme. Je ne puis entrer dans les détails de cette question ; je me contenterai de livrer comme document l'Observation suivante recueillie avec un soin minutieux :

Compression de la moelle de D⁵ à D⁶ (il s'agit du sujet que vous verrez sur un de mes films et chez lequel le niveau inférieur de la compression correspondait à la limite supérieure des réflexes de défense) : Paraplégie incomplète avec contracture en extension

d'intensité moyenne. Hypoesthésie jusqu'à D⁵. Réflexes rotuliens forts, trépidation épileptoïde du pied. Signe des orteils et flexion réflexe du pied très caractérisés. La malade reçoit une heure avant l'opération, en injection sous-cutanée, un centigramme de chlorhydrate de morphine et un milligramme de bromhydrate de scopolamine. Elle est ensuite endormie à l'éther avec l'appareil d'Ombredanne. L'état des réflexes tendineux et des réflexes de défense reste semblable à ce qu'il était précédemment à un moment où l'anesthésie, semblant complète, se traduit par l'abolition du réflexe cornéen, l'abolition presque complète des réflexes pupillaires, l'insensibilité au pincement avec une pince et à l'incision pratiquée pour l'intervention. Pendant vingt minutes, jusqu'au moment de l'ouverture du canal rachidien, la malade étant plongée dans un sommeil profond, les réflexes tendineux et les réflexes cutanés, examinés de deux minutes en deux minutes, ne subissent pas de modification appréciable. Je note seulement que la flexion réflexe du pied obtenue par le pincement de la peau de la jambe est particulièrement lente. le pied, après s'être fléchi, ne revient à sa position de départ qu'au bout de six à dix secondes. La contracture s'atténue progressivement.

Peu de temps après l'ouverture du canal rachidien et excision d'un tissu néoplasique un peu adhérent à la dure-mère, un nouvel examen des réflexes est fait, quatre ou cinq minutes après le précédent. Cette fois, transformation complète : tous les réflexes sont abolis. La pression artérielle qui avait été prise plusieurs fois depuis le début de l'opération et qu'on explore de nouveau à ce moment ne s'est pas modifiée (16 avec la méthode des oscillations). Mais très peu de temps après, la pression systolique, recherchée de nouveau, n'est plus que de 5. A noter que la température rectale mesurée à ce moment est de 38°2 alors qu'elle était de 37°4 au début. Quant à la rigidité musculaire, elle a complètement disparu. En présence de cet état de shock, on met fin à l'opération. Une heure après, les réflexes rotuliens ont reparu, mais ils sont faibles ; les réflexes achilléens restent abolis ; le pincement de la peau de la face dorsale du pied ne provoque aucun mouvement ; l'excitation de la plante du pied détermine une forte extension du gros orteil, la triple flexion du pied, de la jambe et de la cuisse, et une contraction du tenseur du fascia lata. Le lendemain de l'opération le pincement du dos du pied déterminait l'extension des orteils et la flexion réflexe du pied.

* * *

Je vais actuellement étudier les réflexes de défense dans leurs rapports avec les troubles moteurs, la paraplégie spasmodique, la contracture.

Mes observations m'ont conduit à assigner à chacune de ces deux formes de paraplégie, celle en extension et celle en flexion, des caractères cliniques distinctifs, au milieu desquels les réflexes de défense occupent une place importante. Pour donner un aperçu exact des idées que j'ai exposées sur ce sujet, je pense que le mieux est d'extraire d'un travail que j'ai publié en 1912 [5], sur les réflexes tendineux et les réflexes osseux, les passages suivants :

" Je dois m'occuper, en y insistant, d'une variété de contracture sur laquelle j'ai appelé l'attention et qui, étant donné le but que nous visons, mérite d'être décrite. On l'observe surtout aux membres inférieurs et elle est un des éléments constitutifs d'une espèce de paraplégie dont on saisira mieux l'aspect en la rapprochant de la paraplégie spastique d'Erb. Celle-ci, nous le rappelons, se caractérise par les phénomènes suivants : (a) rigidité musculaire en extension, stable ; (b) simple parésie, c'est à dire affaiblissement peu prononcé de la motricité volontaire ; (c) exagération notable des réflexes tendineux avec trépidation épileptoïde du pied, et parfois danse de la rotule ; (d) réflexes de défense légèrement exagérés ou à peu près normaux ; (e) signe des orteils.

" Voici maintenant les caractères de la paraplégie que nous avons en vue. (a) rigidité musculaire en flexion, qui au début cesse par moments d'une manière complète ou presque complète, mais qui plus tard devient stable ; cependant cette stabilité n'atteint guère le même degré que dans la forme précédente, elle est sujette à des variations fréquentes qui résultent des contractions involontaires des muscles des membres inférieurs ; ces contractions sont habituellement lentes ; elles donnent lieu à des mouvements alternatifs de flexion et d'extension avec prédominance d'action des fléchisseurs. (b) motricité volontaire profondément troublée ; il peut y avoir paralysie complète, (c) réflexes tendineux parfois exagérés, mais pouvant être normaux, affaiblis ou même abolis (d) réflexes de défense toujours très forts ; (e) dans la grande majorité des cas, signe des orteils. Ajoutons que la rigidité en flexion, quand elle est devenue stable, se complique presque inévitablement de rétractions fibro-tendineuses.

" Je ne m'étendrai pas sur les lésions qui déterminent cette forme de paraplégie ; qu'il me suffise de dire qu'il s'agit généralement, soit d'altérations scléreuses diffuses de la moelle, soit d'une compression spinale par une tumeur intra-rachidienne, ou par une pachyméningite ; en outre, dans les cas de ce genre, quand ils sont très caractérisés, la dégénération secondaire des faisceaux pyramidaux fait défaut ou bien est très légère, c'est du moins ce qui semble ressortir des observations anatomo-cliniques recueillies jusqu'à ce jour.

" Je reviens à la clinique. La rigidité musculaire de cette forme de

paraplégie constitue bien une contracture ; elle est, en effet, pathologique, due à un mode de l'activité musculaire, et elle est stable, au moins à une période de son évolution. Mais, comme nous venons de le voir, cette stabilité est moindre que celle de la contracture de la paraplégie spastique d'Erb ; elle est entrecoupée en partie de contractions involontaires lentes constituant de véritables mouvements spasmodiques, et, à la phase de début, les troubles méritent moins d'être rangés dans la catégorie des contractures que dans celle des spasmes. Il en résulte que l'épithète de "spasmodique" conviendrait bien plus à cette variété de paraplégie qu'au syndrome dénommé "tabes dorsal spasmodique."

"La contracture dont nous nous occupons a pour substratum anatomique, comme nous venons de le voir, des lésions du système nerveux central ; ces lésions intéressent la voie pyramidale dont la perturbation se manifeste pendant la vie par le signe des orteils et par l'exagération des réflexes de défense.

"Me voici maintenant en mesure de répondre à la question que j'ai posée après avoir montré que la contracture vulgaire, liée à une altération de la voie pyramidale, a des relations étroites avec la surréflexivité tendineuse. Je peux affirmer qu'il existe aussi une contracture—différente, il est vrai, de la précédente par sa forme—déterminée par des lésions nerveuses centrales atteignant les faisceaux pyramidaux, et pourtant absolument indépendante de la surréflexivité tendineuse. En effet, chez les malades qui la présentent, les réflexes tendineux ne sont pas toujours exagérés, tant s'en faut ; ils sont souvent, soit normaux, soit affaiblis, soit même abolis. Les réflexes de défense, au contraire, sont non seulement toujours présents, mais ils atteignent une très grande intensité.

"Mes observations ont été confirmées sur tous les points par plusieurs neurologistes.

"Cette forme de contracture, surtout commune aux membres inférieurs, peut atteindre en même temps les membres supérieurs, où elle offre les mêmes caractères : rigidité avec mouvements spasmodiques, affaiblissement ou abolition possible des réflexes osso-tendineux, réflexes de défense très forts.

"Qu'on la considère aux membres inférieurs ou aux membres supérieurs, ce qui frappe surtout, ce sont ses liens intimes avec les réflexes cutanés de défense dont elle paraît dépendre, comme la forme habituelle de la contracture dépend de la surréflexivité tendineuse. Pour mettre ces traits en évidence et pour donner à chacune de ces formes de contracture—qui peuvent d'ailleurs s'associer—une dénomination qui la distingue, j'ai proposé d'appliquer à l'une le qualificatif de *tendino-réflexe* et celui de *cutané-réflexe* à l'autre."

A côté des formes types, il y a des formes qu'on pourrait appeler intermédiaires où l'on trouve les principaux caractères de la contracture cutané-réflexe (motricité volontaire très troublée, réflexes de défense très forts) bien que les membres inférieurs gardent d'habitude une attitude en extension. Précédemment, j'en ai montré un bel exemple en vous relatant l'Observation d'une paraplégie due à une compression par tumeur et guérie à la suite de l'intervention chirurgicale. Cette dernière forme comporte un pronostic moins sévère que la paraplégie spasmodique en flexion, laquelle correspond à un stade plus avancé de l'affection.

En France, ma manière de voir a été généralement acceptée et dans un article récent M. Foix [16] écrit ceci :

“Contracture d'automatisme médullaire.”—C'est à mon maître Brissaud, dont la mort prématurée fut un deuil pour la neurologie française, que revient l'honneur d'avoir étudié en premier les contractures en flexion ; mais c'est M. Babinski qui le premier en a établi toute l'importance en montrant qu'elles avaient une séméiologie, une signification pathologique complètement différentes des contractures en extension.

“C'est en effet au sujet des paraplégies en flexion que M. Babinski a établi une distinction entre les contractures tendino et cutané-réflexes qui marque une date dans l'histoire des contractures.

“Nous ne chicanerons pas ici M. Babinski sur le mot plus ou moins heureusement choisi de cutané-réflexe. Il est évident que cette contracture n'a rien de cutané, puisque les réflexes qui la caractérisent peuvent être aussi bien provoqués par l'excitation de la sensibilité profonde que par celle de la sensibilité superficielle. Il n'en est pas moins vrai que la contracture en extension est avant tout caractérisée par l'exagération des réflexes tendineux et la faible intensité des réflexes d'automatisme appelés encore de défense. Tandis que la contracture en flexion est caractérisée non seulement par l'exagération considérable des réflexes d'automatisme, mais encore par la diminution ou l'abolition des réflexes tendineux.

“A cette différence de séméiologie répondent des différences profondes d'étiologie, de pronostic, de signification physiologique.

“Voici une malade qui présente précisément cette contracture en flexion. Considérons-la un instant. Nous voyons d'abord quelle est son attitude. Ses jambes sont ramassées vers elle. Examinons-la de plus près. C'est une attitude de raccourcissement. Et ce raccourcissement comporte le triple retrait segmentaire que nous avons déjà deux fois rencontré : flexion du pied sur la jambe, de la jambe sur la cuisse, de la cuisse sur le bassin.

“Poursuivons plus loin notre étude. Les réflexes rotuliens sont faibles, il n'y a pas de clonus du pied. Par contre, ces réflexes d'automatisme sont très faciles à provoquer : voici le phénomène des raccourcisseurs, une ébauche de réflexe d'allongement, un réflexe partiel d'allongement croisé. C'est bien la dissociation décrite par M. Babinski.

“Comment peut-on interpréter cette séméiologie d'abord, cette attitude ensuite ?

“En ce qui concerne les réflexes d'automatisme, leur intensité implique une libération de la moelle inférieure. C'est là un fait qui n'est pas sans importance, car il indique en général des lésions plus profondes que celles qui s'accompagnent de contractures en extension. On voit assez souvent la contracture en flexion se substituer à la contracture en extension. Pendant quelque temps alors, il y a lutte entre les deux tendances et les deux réflexivités. Toujours la victoire de la flexion implique une aggravation de l'état du malade.

“Y a-t-il seulement *libération* de la moelle ? N'y a-t-il pas en outre irritation, *exaltation* de l'automatisme médullaire ? C'est une chose que, pour ma part, je crois, mais il est difficile d'en donner la preuve.”

“Quant à la contracture en flexion elle-même, son aspect indique quelle en est la pathogénie. Elle n'est autre chose, en effet, qu'un phénomène des raccourcisseurs fixé.”

Sauf sa remarque sur le terme cutané-réflexe, M. Foix est à peu près d'accord avec moi. Je ne trouve pas, soit dit en passant, que son objection soit juste : peu importe que les réactions motrices puissent être obtenues aussi par l'excitation des parties profondes ; il suffit que l'excitation de la peau seule puisse y donner naissance pour qu'on ait le droit de dire qu'elles sont cutanées. Mais c'est là un point tout à fait secondaire. Pour le fond de la question, M. Foix confirme mes observations.

Au contraire, les neurologistes anglais, en particulier MM. Walshe et Riddoch, expriment des critiques qui sont peut-être, au moins en partie, la conséquence de malentendus. Si je saisis bien ce qu'il y a de principal dans les idées de M. Walshe sur les réflexes d'extension et de flexion, voici en quoi elles consistent :

Les extenseurs et les fléchisseurs forment deux groupes soumis chacun à une forme spécifique d'activité réflexe ; elle est tonique dans l'un, clonique, phasique, dans l'autre. Le centre de cette activité a pour siège unique les noyaux spinaux, en ce qui concerne les fléchisseurs ; l'activité des extenseurs nécessite, pour se maintenir, la mise en jeu d'un autre appareil réflexe dont le centre occupe le mésocéphale, les noyaux

paracérébelleux probablement (centre des réflexes de posture).—Une lésion cantonnée dans le faisceau pyramidal exalte à la fois l'activité réflexe des extenseurs et celle des fléchisseurs et donne lieu à une paraplégie en extension. Une lésion siégeant au-dessus du mésocéphale ne produirait jamais une paraplégie en flexion.—Au contraire, une lésion de la voie pyramidale associée à une lésion occupant une des parties de l'arc réflexe, ayant pour centre les noyaux paracérébelleux, détermine une paraplégie spasmodique en flexion ; en effet, l'activité réflexe des fléchisseurs n'est pas affectée par l'interruption de cette voie puisque cette activité est d'origine uniquement spinale ; elle est même augmentée, n'étant plus freinée par une force antagoniste. De pareilles altérations donneraient lieu à une exagération des réflexes s'opérant toujours en flexion ; l'extension, quand elle s'observe, n'étant qu'un effet du relâchement des fléchisseurs, ou étant un allongement croisé, toujours secondaire, jamais primitive.—Les réflexes de défense sont d'autant plus forts (période de shock mise à part) que la séparation entre les centres spinaux et les centres mésocéphaliques est plus grande, que la libération de la moelle est plus complète.—Mais, pour qu'il se développe de la contracture, il faut que les muscles aient un certain degré de tonicité que n'atteignent pas, même après la période de shock, les muscles dans les cas de paraplégie consécutive à une section totale de la moelle ; la contracture implique la persistance de quelques connexions entre l'encéphale et la moelle.

A certains points de vue, cette conception pathogénique cadre avec la description clinique que j'ai faite antérieurement de la paraplégie en extension et de la paraplégie en flexion.

Mettons en regard les caractères symptomatiques tracés par moi de ces deux types de paraplégie et les données physio-pathologiques énoncées par les auteurs anglais.

PARAPLÉGIE SPASMODIQUE EN EXTENSION.

(a) Stabilité de la contracture.

L'activité réflexe des extenseurs est à forme tonique

(b) Réflexes de défense légèrement exagérés ou à peu près normaux

L'activité réflexe des fléchisseurs a pour antagoniste celle des extenseurs.

PARAPLÉGIE EN FLEXION.

(a) Instabilité relative de la contracture avec variations fréquentes liées à des mouvements alternatifs de flexion et d'extension et avec prédominance d'action des fléchisseurs.

L'activité réflexe des fléchisseurs est à forme clonique phasique.

(b) Exagération notable des réflexes de défense.

(c) Motricité volontaire profondément troublée.

(d) Les dégénérations secondaires peuvent être très faibles ou nulles.

L'activité réflexe des fléchisseurs n'est plus freinée par une force antagoniste.

Les réflexes de défense sont d'autant plus forts que la libération de la moelle est plus complète.

Pour que la paraplégie en flexion avec contracture se développe, les connexions entre la moelle et l'encéphale ne doivent pas être complètement rompues.

Mais il est certain qu'il y a aussi des divergences pouvant résulter de ce que le sens des termes employés n'a pas été suffisamment précisé. Il me semble que MM. Walshe et Riddoch, tout en reconnaissant l'intérêt qu'il y a à distinguer la paraplégie en extension de celle en flexion et en rappelant mes travaux sur cette dernière, n'ont pas bien saisi mes idées et qu'il y a là une confusion. Pour eux, la paraplégie spasmodique en flexion est réalisée quand à une paraplégie, serait-elle flasque, s'associent des réflexes de défense amenant la triple flexion, et c'est dans les cas de section complète de la moelle qu'on en observerait les exemples les plus typiques. Or, dans ma description de la paraplégie en flexion, j'ai fait intervenir l'élément *raidéur* (contracture cutanéoréflexe) ; cette rigidité, il est vrai, peut céder par moments au début ; mais plus tard elle devient relativement stable. C'est ce type que j'ai toujours eu en vue, celui d'ailleurs que d'autres neurologistes ont observé après moi et qu'on rencontre encore assez souvent dans la pratique habituelle, les cas de section totale étant tout à fait exceptionnels.

J'estime être en droit de maintenir mon opinion suivant laquelle ce type de paraplégie en flexion, avec contracture, réflexes de défense extrêmement exagérés, exagérés au maximum, est d'habitude liée à des compressions, des lésions scléreuses diffuses sans dégénération secondaire ou avec dégénérations secondaires minimales, ce qui ne veut pas dire que cet état soit incompatible avec des dégénérations secondaires marquées. A cet égard, les observations nouvelles, de guerre, si intéressantes qu'elles soient, n'infirmement aucunement les observations anciennes.

Contre l'opinion de M. Walshe et de ceux suivant lesquels une lésion siégeant au-dessus du mésocéphale ne produirait jamais une paraplégie en flexion, on peut faire valoir l'Observation rapportée par MM. Pierre Marie et Foix [24] et intitulée : "Paraplégie en flexion d'origine cérébrale par nécrose sous-épidymaire progressive."

"Notre cas, disent les auteurs, est, croyons-nous, le premier cas anatomo-clinique de paraplégie en *flexion* d'origine cérébrale; en tout cas, le premier dans lequel on ait observé la dissociation signalée dans certains cas par M. Babinski entre les réflexes d'automatisme dits de défense et les réflexes tendineux.

"Ceci est une notion importante au point de vue physiologique, car il n'existait pas chez notre malade de lésions mésocéphaliques, mais simplement une double lésion cérébrale. La suppression de l'influence des centres mésocéphaliques n'est donc pas indispensable pour que se produise l'automatisme médullaire et la paraplégie en flexion. Il n'est pas nécessaire non plus qu'il y ait lésion irritative comme dans le cas déjà signalé de M. Babinski (paraplégie en flexion par compression mésocéphalique); une simple lésion destructive suffit, en supprimant l'influence cérébrale."

A ce sujet, je rappellerai que dans mon travail de 1911 sur la Paraplégie spasmodique avec contracture en flexion, j'écrivais ceci, p. 135 : "Des lésions bilatérales de l'encéphale semblent pouvoir donner naissance à un syndrome analogue" [3].

Il faut s'attendre à la publication de nouvelles observations et à de nouvelles discussions. Le dernier mot sur cette question ne paraît pas avoir été dit.

* * * *

Dans une communication intitulée : "De la surréflexivité hyperalgésique" [8], nous avons relaté, Jarkowski et moi, trois Observations de Syndrome de Brown-Séquard, dans lesquelles nous avons été frappés par la présence d'un même phénomène dont voici les traits essentiels : une excitation telle que le pincement de la peau du côté de la lésion, où il y a de l'hyperalgésie, sans être suivie d'aucune manifestation de ce côté, donne lieu du côté opposé à une réaction motrice brusque, en même temps qu'elle détermine des grimaces et une inspiration bruyante (phénomènes analogues aux "pseudoaffectifs réflexes" observés par Sherrington chez les animaux décérébrés).

Dans un travail ultérieur, "Automatisme et hyperalgésie dans l'hémiplégie cérébrale" [9], nous avons relaté les faits suivants : chez certains hémiplegiques présentant de l'hyperalgésie, l'excitation des téguments du membre inférieur est suivie d'une réaction motrice du membre supérieur du côté sain, différente suivant qu'on excite le côté sain ou le côté malade. Dans le premier cas, la main se porte sur le point excité comme pour le protéger. Dans le deuxième, le membre supérieur se soulève, la main se porte sur la tête et vient s'appliquer soit à sa partie antérieure, soit à sa partie postérieure. Dans certains cas, nous avons

été frappés par la constance avec laquelle ces réactions se produisaient. On pouvait à volonté, en pinçant alternativement les deux côtés, faire exécuter à la main saine des mouvements en sens inverse : la main était-elle appliquée sur la tête à la suite du pincement du côté malade, on obtenait son déplacement vers le membre inférieur du côté sain en pinçant la jambe saine ; et si alors on pinçait la jambe du côté malade, le bras s'élevait de nouveau et la main se portait sur la tête.

Ces réactions motrices diffèrent cliniquement de celles que nous avons étudiée dans notre Conférence. Nous les rapprochons des réflexes de défense, mais nous les en distinguons. Les unes et les autres peuvent d'ailleurs être associées.

Nous pensons que les réactions observées chez les malades qui sont l'objet de notre travail sur la réflectivité hyperalgésique sont des réflexes ayant leur centre dans l'encéphale.

Quant aux mouvements de la main vers la tête constatés chez les hémiplegiques dans notre Note sur l'automatisme et l'hyperalgésie, nous sommes portés à croire qu'il s'agit là d'un acte automatique déclenché par la sensation spéciale qui résulte de l'hyperalgésie, sensation nouvelle, non encore éprouvée, insolite et occasionnant ainsi une surprise, un état d'anxiété que traduit la physionomie du malade, bien que sa conscience puisse être considérablement amoindrie.

Nous avons cru devoir signaler ces phénomènes dont on trouvera la description détaillée dans nos publications. Mais nous n'y insisterons pas davantage, faute de temps et parceque, en le faisant, nous sortirions des limites de notre programme.

* * * *

Je me suis proposé de traiter dans cette Conférence la question des réflexes de défense surtout en clinicien, en neurologiste. Je ne crois pas cependant pouvoir la terminer sans vous dire quelques mots du mécanisme de ces réflexes, dont il a été déjà question, du reste.

Vous avez vu que MM. Marie et Foix ont insisté sur la présence des réflexes d'extension croisée observés par eux chez certains sujets atteints de lésions de la voie pyramidale. Les rapprochant du "crossed extension reflex" de Philipson, ils arrivent à cette conclusion que les mouvements réflexes dits de défense sont des mouvements du même ordre que les mouvements du stepping reflex et constituent des manifestations de l'automatisme spinal de la marche. Les neurologistes anglais contestent l'exactitude de cette conception ; ils soutiennent que chez l'homme, dans les sections totales de la moelle, les excitations nociceptives d'un côté, quand elles provoquent l'activité des extenseurs du côté opposé, ne

donnent lieu qu'à des contractions légères sans déplacement des divers segments du membre, et que les mouvements alternatifs rythmés qu'on observe chez le chien spinal font ici défaut.

M. Foix, dans une publication récente à laquelle j'ai déjà fait des emprunts, semble faire quelques concessions tout en maintenant en grande partie son opinion première. "Il est possible, dit-il, que l'automatisme de défense entre pour une part dans la pathogénie de ces réflexes, mais, pour la majeure part, ils se rattachent à l'une des fonctions essentielles de la moelle, c'est à dire à l'automatisme de la marche"

J'ai cherché précédemment à faire ressortir la distinction capitale qu'établissent les auteurs anglais entre le groupe des fléchisseurs et celui des extenseurs soumis chacun à une forme spécifique d'activité réflexe : les réflexes d'extension seraient des réflexes de posture ; les réflexes de flexion seraient des réflexes cloniques, phasiques. C'est dans le groupe de ces derniers réflexes que rentrent pour la plus grande part ce qu'on appelle les réflexes de défense.

La conception fondamentale des neurologistes anglais, issue des idées de Jackson, de Sherrington, est que ces réflexes de flexion tels qu'on les observe à l'état pathologique traduisent la libération de la moelle par rapport aux centres supérieurs.

Les faits observés cadrent fort bien pour la plupart avec cette conception. Toutefois, sans en contester la justesse, on peut se demander si, dans la genèse des phénomènes en question, l'élément "irritation" ne peut pas jouer aussi un certain rôle

C'est une idée que M. Foix tend à admettre, comme on l'a vu précédemment.

Ce fait que les réflexes de défense n'avaient paru dès mes premières observations particulièrement intenses dans les cas de compression de moelle et de sclérose spinale sans dégénération secondaire m'avait déjà conduit autrefois à cette même idée.

A l'appui de cette manière de voir on peut invoquer encore d'autres faits sur lesquels nous avons déjà insisté. On peut observer parfois—nous le rappelons—des sujets atteints de lésions spinales qui, après avoir présenté une paraplégie plus ou moins marquée, paraissent complètement rétablis. la motricité est redevenue normale, la sensibilité est intacte, il n'y a pas de perturbation des sphincters, et cependant il y a persistance très nette du signe des orteils et de la flexion réflexe du pied. Sauf ces derniers phénomènes, le fonctionnement du système nerveux semble absolument normal. Est-il permis de soutenir en pareil cas qu'il y a libération de la moelle ? Ce ne serait alors qu'une libération relative aux réflexes de défense. L'état pathologique de ces réflexes ne se

comprendrait-il pas mieux dans des cas de ce genre si l'on admettait qu'il est sous la dépendance de l'irritation des centres nerveux produite par le reliquat de la lésion ?

Considérant maintenant la question d'un autre point de vue. je soumettrai quelques idées à vos réflexions.

Au début de cette Conférence, j'ai tracé un parallèle entre les réactions motrices consécutives aux excitations périphériques suivant qu'elles sont pathologiques ou physiologiques. Il résulte de ce que j'ai dit que les premières peuvent être considérées comme l'exagération des secondes, ou plutôt les secondes comme la réduction des premières : de part et d'autre, en effet, on observe le phénomène de la triple flexion avec contraction du tenseur du fascia lata ; mais ce qu'il y a de spécial aux réactions physiologiques c'est qu'on ne les obtient que par l'excitation de la zone plantaire et que les mouvements sont plus rapides et moins amples. A l'état pathologique, la triple flexion (seul mode de réaction que j'envisage ici) semble bien pouvoir être interprétée comme un retour à un état ancestral : la partie excitée fuit l'objet vulnérant (retrait du membre, raccourcissement) et une excitation peut déterminer, loin du point où elle a eu lieu, un mouvement de fuite ; c'est ainsi que la triple flexion peut être provoquée par excitation de l'abdomen ou du thorax. A l'état physiologique, ces réactions ancestrales se sont maintenues, mais ont subi des modifications importantes. Comment le comprendre ? On pourrait dire que lorsque les centres supérieurs ont asservi les centres inférieurs, ceux qui correspondaient aux centres spinaux, ils ont inhibé les réactions susceptibles d'être nuisibles à l'individu et ont laissé subsister, en les adaptant à ses besoins, celles qui sont capables de lui servir. Or, il est évident que la triple flexion consécutive à une excitation de la jambe, de la cuisse ou de l'abdomen ne pourrait avoir que des inconvénients ; cette réaction a donc été supprimée. Que sous l'influence d'une irritation nocive de la plante du pied continuellement en contact avec le sol, la triple flexion s'opère, même indépendamment de la volonté, cela ne peut être qu'utile ; cette réaction a donc été conservée. Mais il y a intérêt aussi, au point de vue de la marche, à ce que la réaction ne soit pas de longue durée ; aussi la décontraction est-elle rapide au lieu d'être lente. On saisit ainsi les raisons pour lesquelles, à l'état physiologique, les réactions motrices qui me paraissent ressortir aux réflexes de défense, s'effectuent avec rapidité et ne se produisent que lorsque les excitations portent sur la région plantaire.

Il me semble intéressant de rappeler à ce propos que dans les sections totales de la moelle, après la période de shock, lorsque les réflexes

cutanés reparaissent, la région plantaire est seule réflexogène pendant un certain temps.

Comparons maintenant le réflexe des orteils aux réflexes précédents. Si à l'état pathologique la réaction habituelle des orteils, l'extension, peut être rapprochée, en ce qui concerne son mécanisme, de la triple flexion, à l'état physiologique le mouvement des orteils, la flexion, semble avoir une autre signification que la triple flexion du pied, de la jambe et de la cuisse. M. Riddoch fait observer que la flexion réflexe des orteils fait partie du stepping-reflex, et qu'elle accompagne l'extension de la cuisse, de la jambe et du pied. Mais il est à remarquer qu'à l'état physiologique chez l'homme, l'excitation de la plante du pied, qui provoque la flexion des orteils, détermine du même côté la triple flexion du membre inférieur et il en résulte une quadruple flexion. Cette flexion des orteils ne serait-elle pas aussi le témoin d'une réaction ancestrale, ayant apparu toutefois à une période du développement plus avancée que les réflexes de défense dont il a été précédemment question, période où les orteils servaient de griffe? Cette réaction avait aussi en partie la protection pour but, mais c'était un mode de protection différent de celui qui est réalisé par les réflexes de défense primitifs; il ne s'agit plus d'une fuite localisée, d'une retraite en face d'une offensive; ce mouvement de griffe vis à vis d'une agression constitue une contre-offensive, mode de protection d'un ordre plus élevé; on conçoit du reste fort bien qu'un animal cherchant à se défendre combine l'attaque avec la fuite. On saisirait ainsi la quadruple flexion à l'état physiologique: la flexion de la cuisse, de la jambe et du pied ressortissant aux réflexes de défense primitifs, la flexion des orteils étant l'expression atavique d'un réflexe de préhension.

Cette conception permettrait de comprendre pourquoi l'extension des orteils n'est pas toujours associée à la triple flexion; suivant que dans le domaine des orteils, le réflexe de fuite l'emportera, ce qui est la règle à l'état pathologique, sur ce que nous appelons le réflexe de préhension, ou bien sera dominé par lui, on obtiendra l'extension ou la flexion des orteils.

Je rappellerai à ce propos que M. van Woerkom, dans le travail cité plus haut, fait ressortir que "le gros orteil est construit dans certains stades de la vie intra-utérine pour remplir une fonction de préhension." Cet état qui chez les autres primates est perpétuel, est passager chez l'homme.

Est-il nécessaire d'ajouter qu'il s'agit là pour une grande part d'hypothèses!

* * * *

Dès le début de mes recherches sur le phénomène des orteils, j'avais eu l'occasion de le constater chez des nourrissons, et il m'avait semblé

qu'il persistait approximativement jusqu'à la période où l'enfant commence à marcher, ce qui s'explique quand on se rappelle quel est l'état du système pyramidal à cette époque de la vie : on peut dire que l'enfant est atteint d'une paraplégie—curable—comme on peut dire aussi que chez lui la moelle n'est pas encore sous la domination de l'encéphale.

D'après Léri [20], à la naissance l'extension des orteils est la règle ; la flexion l'exception. L'extension disparaît en général, chez l'enfant normal, vers 5 ou 6 mois, mais il y a des variétés individuelles : il peut y avoir une période de transition assez prolongée, marquée par des alternatives de flexion et d'extension et souvent par l'extension unilatérale.

Des recherches nouvelles de Bersot [12], de Lantuejoul (communication orale) ont montré qu'il y avait lieu de rectifier un peu les données précédentes : à la naissance, puis pendant un laps de temps d'une durée assez courte, les orteils réagissent en flexion et ce n'est qu'ultérieurement que l'extension apparaît. Cela surprend d'abord, mais n'est pas contradictoire si l'on admet que la flexion des orteils, réaction physiologique il est vrai, est le reliquat d'une réaction ancestrale et si l'on se rappelle que chez l'adulte on peut observer un réflexe en flexion chez des sujets atteints de lésions avérées de la voie pyramidale.

En ce qui concerne la flexion réflexe du pied, on la constate aussi chez l'enfant, ainsi que l'a établi une de mes élèves, Mlle Rosenblum, qui a fait de cette question l'objet de sa Thèse inaugurale ; mais l'extension du gros orteil subsiste d'habitude plus longtemps que la triple flexion.

Je vous signale avant de terminer un travail de M. Minkowski ayant pour titre : " Sur les mouvements, les réflexes et les réactions musculaires du fœtus humain de 2 à 5 mois, et leurs relations avec le système nerveux fœtal " [25].

J'extrais de cet article (p. 1113) le passage suivant : " On peut dire en général que chaque partie des téguments peut servir de zone réflexogène à des réactions motrices très variables, proches et lointaines, ayant la tendance à se généraliser plus ou moins à tout l'organisme fœtal."

Cette donnée est à rapprocher de ce que nous avons dit précédemment sur la possibilité de provoquer parfois, à l'état pathologique, des réflexes des orteils et du pied en excitant les téguments de l'abdomen et du thorax.

Messieurs, comme vous venez de le voir, l'étude des réflexes de défense soulève des problèmes de phylogénie et d'ontogénie, et à cet égard elle est déjà fort intéressante ; mais elle l'est surtout pour le neurologiste. Ces réflexes constituent un chapitre important de la pathologie du système nerveux.

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A STUDY OF THE SHERRINGTON DECEREBRATE ANIMAL IN THE CHRONIC AS WELL AS THE ACUTE CONDITION.

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¹ In general the experimental work was done by H. C. B., and Chapters II, III and VI (b) were written by him. The semi-decerebrations and all the anatomical examinations were made by W. G. P., and Chapters IV, V and VI (a) were written by him.

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INTRODUCTION.

THE researches on which this paper is based were commenced originally in a search for a preparation which would allow experiments on the origin of surgical shock, and also on the effect of temperature on the resistance to infection in animals not under an anæsthetic and yet without there being any possibility of pain. The Sherrington preparation seemed ideal for this purpose, since the question of any conscious sensation could be completely excluded, and in addition the preparation would remain quiet during experimentation. The main object has, therefore, been to develop a technique which would allow the preservation of the decerebrate animal for many days, in spite of the removal not only of the cerebrum, but also of the basal ganglia and most of the mid-brain. This has necessitated the use of 124 animals, and in the course of the work some points of interest have arisen in connection with the reflexes and the histological anatomy. In many experiments our data are not as complete as we would have wished, but it was found that the process of examining the animals diminished their chance of survival and consequently the observations had to be curtailed, if the main object of the research was to be attained.

In spite of these difficulties a certain number of important facts were demonstrated. One of the most noticeable was the very remarkable similarity between the decerebrate preparations which had been kept "alive" for two or three weeks, and the acute preparations described by Sherrington on examination an hour or so after the operation. The decerebrate rigidity often continues (with only brief intermissions) for weeks, so that there can be no possibility of the condition being due to stimulation of the cut nerve fibres at the site of operation, and since in this time the damaged nerves are undergoing degeneration it is possible to exclude definitely some structures from any participation in this reflex. On the other hand, the chronic preparations do show certain

definite differences from the acute; for instance, after the first two or three days a small percentage of the animals will occasionally make definite sounds, and these sounds appear to be reflex since they occur usually as the result of some definite stimulus. The most common of these sounds was purring occurring immediately after the stomach had been filled with milk by a stomach tube; while mewling has only been observed in two animals, and in these it occurred only once or twice and could not be made to recur by applying stimuli which would be painful to a conscious animal.

Extensive histological studies have only been possible on a few of the preparations, but in these the results are of interest since we believe that never before have preparations been maintained in a sort of life so as to allow degeneration to occur after such complete removal of all the higher nervous centres. In many other cases the nervous tissue was useless for detailed examination as the result of incubation for some hours after death and consequent rapid post-mortem changes.

CHAPTER I—HISTORICAL NOTE ON DECEREBRATION.

The method of removing parts of the brain in order to study function in the central nervous system has been employed since Rolando's experiments on birds in 1809. Flourens, indeed, succeeded in keeping pigeons alive for months after the removal of the fore-brain. But Longet [32], in 1842, first discriminated carefully as to what brain structures he actually removed. He noticed that many "reactions" remained if he removed all of the brain down to and including the colliculi—"choses remarquables!"; but that after removal of the pons all reactions disappeared, excepting only respiration and circulation.

Goltz kept three decerebrate dogs alive for months. The brain-stem of one animal most carefully studied was examined by Gordon Holmes [21], who found that a considerable amount of thalamus and all the cranial nerves were intact, although there seemed to be some softening of the corpora quadrigemina. There was no loss of temperature control and the animal shivered in a cold room. It could walk and would eat when brought close to food. Rothmann [51] [52] likewise produced a chronic preparation, a dog from whom all or most of the brain above the optic thalamus was removed. This animal ate and drank normally, walked and ran and showed a limited ability to learn. He likewise had normal temperature control and apparently normal muscle tone. Karplus and Kreidl [25] extirpated the hemispheres of monkeys and

kept one alive as long as twenty-six days. More recently, Dusser de Barenne [2] has kept one cat alive six months, and another animal eleven months, after removing the fore-brain. A careful examination by Brouwer [7] of the post-mortem material showed the thalamus, mid-brain, and rhinencephalon to be intact in one, and most of the thalamus and mid-brain in the other. These preparations did not show decerebrate rigidity and were able to maintain a normal temperature. Only the animal with a portion of the fore-brain intact would eat spontaneously.

As indicated briefly above, in all previous *chronic* decerebrate preparations much of the thalamus was intact as well as the mid-brain. The animals possessed normal temperature control and have been able to execute complicated co-ordinated movements.

Decerebration at the level of the mid-brain was shown by Sherrington in 1896 to produce "decerebrate rigidity." This condition in *acute* preparations has been the subject of much study since that time by Horsley, Thiele, Weed, Magnus, Cobb, *et al.* Their conclusions will be discussed in another part of this communication. Recently, signs and symptoms in a group of patients considered to be analogous to decerebrate animals have been described by Wilson [63]. Riddoch and Buzzard [49] have also described such symptoms in man.

Boyce [6], in 1895, removed the brain on one side down to the middle of the mesencephalon and kept the animals (cats) alive as chronic preparations. His principal interest was in the descending degenerations thus produced. Probst [46], in 1904, made sections through one lateral half of the mid-brain without removing any tissue and studied the general behaviour of the animals as chronic preparations.

This brief sketch makes no pretence to enumeration of all of the valuable contributions to neurology made by this experimental method. In general, preparations produced by decerebration at higher levels and extending down as far as the medulla oblongata have been studied as *acute* experiments. In the case of all previous *chronic* experiments, the level of removal has been at least well above the mid-brain and most of the thalamus.

CHAPTER II.—TECHNIQUE.

The animals used have been cats in all cases. The general procedure has been to decerebrate the animals aseptically under an anæsthetic and then to keep them under conditions which will maintain by artificial means their temperature constant. In the main

the technique has followed the lines described by one of us (H. C. B.) [4] in a preliminary communication,¹ but as it has been modified in details it will be advisable to give here a full description. The whole process is founded on Sherrington's original (and older) method developed in 1896 [53] [54].

(a) *Operative*

Pure chloroform has been used as the anæsthetic since we have had no success with ether. The preparations have considerable difficulty in getting rid of mucus and this probably accounts for the difficulties we have had. Subcutaneous injection of 0.5 mgm. of atropine has been given immediately after induction of anæsthesia in some animals, perhaps with beneficial effect. During the actual decerebration a total cessation of respiratory movements for a short while is not uncommon, and causes the loss of some animals. To overcome this intratracheal insufflation has been tried both with chloroform and ether. With chloroform insufflation we have had some success, but the greater irritation to the trachea and the consequent risk of infection seem to more than counterbalance the diminished risk of the actual operation. Cessation of respiration is less liable to occur if the animal is deeply anæsthetized at the time the section is made, so that with a good anæsthetist trouble of this kind is rare, even with an ordinary inhalation method, and it is this that we have mostly used.

The skin on the back of the head is shaved, cleaned and painted with an alcoholic solution of iodine, and in the later technique the animal is then turned over and the front of its neck is also shaved. A small incision is made (1 to 2 cm. in length) in the mid-line at the level of the thyroid cartilage, and from this both carotid arteries can be reached; a thick ligature is passed around each of them, and is then tied to form a loop so that traction can be made on the vessels to obstruct the blood-flow as desired. These two loops are brought out through the middle line and then the wound is closed with two or three waxed silk sutures. Hæmostat forceps hanging on these loops during the actual process of decerebration will prevent most of the bleeding and allow much more accurate work. It does not seem necessary to take any aseptic precautions after this neck wound has once been stitched up, and we have had no serious infection of these wounds.

The animal is then again turned over and an incision made on the

¹ In the protocols "earlier method" indicates that the operation was performed as described in this communication.

back of the head. A skin flap is turned back on one side, the temporal muscle is separated from the bone, the skull is trephined and the hole enlarged to a good size. While the actual decerebration is performed the weights on the carotid are allowed to hang free and constrict the vessels and the anaesthetist compresses the vertebral arteries just below the transverse processes of the atlas. The dura is opened and with a blunt spatula the occipital lobe on the near side is removed so as to bring into view the corpora quadrigemina. The division across the brain-stem can then be made at any desired level; this is done with the same blunt spatula, carrying the cut right through the brain to the base of the skull. It has proved much more satisfactory to make absolutely certain of preserving the pituitary gland intact, as will be explained later, and this has been attained most easily by the careful choice of the plane of the section and by carrying a horizontal cut forwards with a specially bent and rather blunt scalpel, starting from the transverse incision and passing forwards through the base of the brain a millimetre or two above the level of the pituitary. The whole of the brain matter above these two cuts is then scooped out and the cavity is lightly plugged with cotton wool. After this the vertebral arteries may be released and a little later the carotid blood-flow may be allowed to return. The whole procedure of removing the brain should only take about a minute or two.

The packing in the cavity is left for five or ten minutes and is then carefully removed. If there is any bleeding a small pad of muscle is put over it and packing is repeated and maintained for another five minutes. When the cavity is quite dry the closing of the wound is commenced. It is important to obliterate the large dead space of the cranial cavity in order to minimize the chance of infection. This has been done usually by filling it with a mixture of equal parts of vaseline and paraffin wax (melting 55° C.), the mixture setting at about 45° C. It is sterilized by heating to 140° C. for three-quarters of an hour on three successive days. If the hæmorrhage has been difficult to stop it is usually safer first to spread over the base of the skull a thin layer of gauze soaked in saline, the end of the gauze protruding through the wound, the temporal muscle being split vertically so as to make this easier, and then pour in the wax at a temperature of about 47° C., allowing it to set in the cranium. The wax does not stick to the wet gauze, so that when the wax is set the gauze may be gently withdrawn, or if hæmorrhage is feared it may be left in place until the following day. In the latter case a corner of the gauze may either be allowed to

protrude through a counter-incision in the skin, or it may be just beneath the skin which has been closed by a suture above it, so that on the next day the stitch may be removed and the gauze withdrawn without any trouble. It is probable that it is best to leave always a little gauze in place while the wax is setting, since on removal it leaves a small cavity and so allows room for some swelling of the remaining parts. In the earlier experiments where the whole brain matter to the level of the tentorium was scraped away trouble from this factor was not conspicuous, but with the modification of the operation as here described a post-operative rise in intracranial pressure may play a more important rôle.

In the few animals in which only one hemisphere has been removed the use of wax has proved unsatisfactory, probably owing to the much greater chance of swelling of the remaining parts in these animals. In the unilateral decerebrations in consequence the cavity has been merely filled with saline and it is conceivable that this might also be satisfactory even in the complete decerebrations. The other variations in the technique in the unilateral operation are described later (Chapter IV), since all these animals have been operated on by W. G. P. An attempt has also been made to get rid of the dead space in the animals by removing the whole cranial vault and drawing together the two temporal muscles over the base of the skull. Unfortunately it is not possible to make these muscles cover the space completely, nor is it possible to leave a smooth surface at the base of the skull without opening the nasal sinuses, and in our experience this had led to an infection of the wound with a regularity not seen in the paraffin method. For experiments lasting only three or four days, however, it is satisfactory.

The main difference between the later technique and the earlier one previously described is the horizontal section just above the level of the pituitary gland, allowing the blood-supply of this gland to remain intact. The contrast between the two methods may be seen by reference to figs. 9 and 10, which show photographs of a brain-stem operated on by the later method and comparing with them fig. 22, which illustrates the brain-stem left by the older technique. As in the earlier experiments the stalk of the gland was cut across, the blood-vessels supplying the anterior lobe must have been divided, and the gland itself may easily have been damaged and perhaps subjected to some pressure. In spite of this several animals survived for periods of two or three weeks, but as a rule they would not live more than three or four days. In these death was preceded usually by convulsive movements without signs of

infection, or else was due to broncho-pneumonia. The convulsions occurring within three or four days were apparently similar to those described by Cushing [12]. [13] as the result of removal of the pituitary, and consequently the modified operative technique was developed. This necessitates a more ragged incision with greater hæmorrhage, so that temporary control of the carotid arteries had to be also adopted. Following this change in the technique death on the third or fourth day preceded by convulsions has no longer been seen, and the animal's resistance to broncho-pneumonia has also seemed greater, but on the other hand, many more animals have been lost during the first day from reactionary hæmorrhage, and infection of the wound itself has also been more common.

The later technique has also given rise to some trouble, since the changed slope of the section has often been overdone, resulting in damage to the fifth nerve. Such damage must be avoided since it leads to the development of ophthalmia and pressure sores around the mouth, complicating the nursing and greatly increasing the risk of broncho-pneumonia.

(b) *Post-operative.*

The wound requires no covering, especially if it be stitched with waxed silk to prevent infection tracking inwards along the sutures, which may otherwise occur if the animal be kept in a bath. The wound may be left dry or covered with mercury ointment.

The main difficulty to be overcome is the maintenance of a constant temperature. For the most part the animals have been kept in a water bath, through which water was kept circulating and in which they were supported on a sling three-quarters immersed in the water. Stirrers maintained a constant mixing of the water, and a thermostat regulator maintained the bath with a variation of only 0.2 to 0.4 C. in twenty-four hours at its best. Unfortunately, it often fell below this standard, as owing to post-war conditions the gas pressure sometimes fell so low as to be incapable of heating the large volume of water circulating through the bath.

In a bath the preparation readily gains heat from or loses heat to the circulating water, so that its rectal temperature rarely differs from that of the bath by more than 1° C. and practically never by more than 1.5° C. The bath has been usually kept at a temperature between 38° and 39.5° C. This method is possibly the simplest that will allow the maintenance of a constant body temperature in a preparation where

the metabolism shows rapid variations, as it must in any which happen to show strong running reflexes. No ill effects from the prolonged immersion in water have been seen, even after two or three weeks, except a gradual shedding of the hair.

The disadvantages of the bath method are obvious, and it is this method that is mainly responsible for the paucity of our observations on the reflexes. Rough examination of the animal is possible as it is turned each day in the bath to avoid pressure sores, but in order to make any careful examination, it has to be taken out, washed in hot water, washed again with alcohol, roughly dried with a towel and finally dried in a hot incubator. Even with this technique, which requires four or five hours, the body temperature is apt to drop to 35° C. or lower, and though no ill results are noticed at the time, pneumonia often supervenes. Consequently any such examination will greatly decrease the preparation's chance of survival.

Owing to this many attempts have been made to keep them in an incubator. An ordinary incubator is useless, since the heat loss varies with the moisture in the air. Haldane [18] has shown the importance of the wet bulb temperature, but even an incubator controlled on a wet bulb basis is insufficient. The reason for this is that a very exact balance between heat loss and heat production has to be attained in these animals, and once this balance is upset the discrepancy tends to grow, since it is probable that in these preparations the metabolism falls with fall of body temperature instead of showing a compensatory increase. An incubator method has, however, proved possible by using an incubator heated by live steam escaping within it, so that heating occurs through condensation on its walls. In this way the wet and dry bulb temperatures are identical, the air being completely saturated with moisture. Even in such an incubator the control has to be altered during the first few days to match the gradual loss of the insulating action of the fur as it becomes penetrated with moisture, or this variation must be overcome by destroying these heat insulating properties of the fur by soaking the animal immediately after operation in petroleum oil. Under these conditions the animal loses heat mainly by radiation and conduction and usually keeps a rectal temperature about 4° C. above that of the incubator, so that this should be kept at about 34° or 35° C. The proper mixing of the air is ensured by an electrically driven fan. Further details of incubator experiments are given in Chapter III.

Food is given twice a day by stomach tube, a full-size cat requiring

about 100 c.c. of milk at each feed. Great care must be taken to keep the mouth, eyes and nose clean, and the animal must be placed in a position which would be comfortable if it were conscious.

The chief causes of failure are infection, usually respiratory, less commonly infection of the wound, post-operative hæmorrhage, and in the earlier technique probably also pituitary insufficiency. No testicular atrophy nor adiposity has, however, been observed. One animal (previously reported) lost 10 per cent. of its weight in a week, but another (cat II) after twelve days "life" showed no change whatever in its body weight. Further experiments on the functioning of the pituitary in these animals are planned.

The prevalence of pneumonia in these preparations is of some interest in that it was commoner if the animals had been previously exposed to conditions giving them a low body temperature, even if this occurred a considerable time after their anæsthetization. An instance of this is seen in the case of cat II, which is described later.

CHAPTER III.—CHRONIC DECEREBRATE PREPARATIONS.

(a) *Details of Two Preparations.*

The characters shown by these animals can be best illustrated by recording a few examples in more or less detail and then giving a more general description. The question of the individual peculiarities in relation to the exact site of the section is a difficult one and will be considered later.

Animal I.—Young castrated male. Post-mortem examination, p. 239. 0.5 mgm. atropine subcutaneously after anæsthesia induced. Right carotid tied, left occluded temporarily. Trouble from hæmorrhage which was eventually stopped after using a cautery and leaving in muscle and cotton-wool plugs. Some cotton left in under wax. Section by the later technique with preservation of the vascular supply to the pituitary. Kept on a warm table for three hours it developed a hæmatoma from reactionary hæmorrhage during this time. Five hours after operation when in bath had moderate rigidity¹ and moderately brisk pinna reflexes. Bath temperature 39.4° C. Rectal temperature 39.8° C.

Second day. Conditions much the same. Good corneal reflex on left side but none on right.

Third day. Condition much the same. Respiration rate only 17.

Fourth day. All reflexes more sluggish. Rigidity still fair.

Fifth day. Reflexes as before. Rigidity stronger and fore paws kept

¹ Rigidity refers to the extensor rigidity of the limbs described in decerebrate preparations by Sherrington unless otherwise stated.

extended and held rather backwards towards the tail. When turned on mattress slight kicking and extrusion of claws. Bath temperature $39^{\circ}2'$ C. Rectal temperature $37^{\circ}8'$ C.

Seventh day. All reflexes more brisk. Rigidity fairly good. Respiration rate 19. Sores developing in mouth.

Ninth day. Pinna reflexes more brisk. Vigorous shaking of the head now present on blowing in the ear. Licking of lips and nose now present after feeding. Rigidity very variable, being either very good or else animal in flexed and fairly flaccid condition.

Eleventh day. Reflexes still improving. Rigidity almost absent in the morning but on turning the animal it became extremely marked. The limbs are moved somewhat if the pinna is twisted. If traction is exerted on the front paws there is a movement of retraction and flexion of the limb with extrusion of the claws.

Thirteenth day. Ophthalmia of the right eye now well advanced. Rupture of cornea. Condition as before, but when lying on left side has a position in which the fore limbs are rigid and extended (left more than right) and in which the left hind limb was also rigid and extended, but the right hind limb was rigid in a flexed position. Hind limbs now show retraction when pulled upon as well as the fore limbs, but there is no extrusion of claws in the hind limbs. If animal is stimulated by twisting the ear the head is raised, being bent either to the left or right according to which side it is lying on. No acoustic reflex present now or at any other time.

On fourteenth day as before. Crossed reflexes easily obtained in hind limbs. If right limb is forcibly flexed it stays flexed and then on pinching left limb the left is flexed and right extended and vice versa. On cleaning the left eye the animal moves its head, extending it dorsally as though objecting. General appearance of movement is that of a pseudodffective reflex.

Fifteenth day. Respiration rate 12 only.

Seventeenth day. Respiration rate 16. Reflexes much as before but very variable.

Eighteenth day. Found dead.

Animal II.—Female. Post-mortem examination, p. 247. Weight, 2.45 kilos. Old method used and the cranial cavity scraped clean to the tentorium. Kept in incubator for one hour and then put into bath. Eight hours later fed, 100 c.c. of milk. Rigidity then good and pinna reflexes and corneal reflexes brisk. On following day these reflexes still brisk, respiration rate 20, bath temperature $39^{\circ}2'$ C., rectal temperature $38^{\circ}1'$ C.

After two days reflexes more brisk. Acoustic reflex now present; animal shakes its head slightly in response to loud noises.

Fourth day. Reflexes not quite so brisk; rigidity still good.

Fifth day. Vomited after the morning feed.

Sixth day. Reflexes much more brisk and rigidity very good. When lying on right side moves head slightly when hands are clapped; with high note of

a whistle lifts head up from the rest, bending it to the left. When lying on left side acoustic reflex scarcely noticeable, since the head is pressed downwards to the left.

Seventh day. Reflexes much more brisk, especially acoustic. If lying on right side now lifts head well up when anyone walks into the room, unless on tiptoe. Very brisk response to slight scratching noises. Pushes head downwards as before in response to sounds if lying on the other side.

Eighth day. Bath outlet choked. Animal taken out and dried during cleaning of the bath. During the drying, temperature fell to about 34° C. and remained subnormal about two hours. Weight when dry 2.4 kilos. Rigidity fairly good but not so strong as previously, and animal does not remain well in a sitting position as do most preparations. Acoustic reflex confined to head and neck movements. On touching the animal running movements are developed with strong movements of the front limbs and only slight in the hind limbs. Returned to the bath after eight hours.

Ninth day. Keeps eyes open, though previously they have been kept shut. On whichever side it is lying the upper fore limb is held passing forwards and downwards across the other, the lower fore limb passing somewhat backwards and upwards. This position is a very characteristic one and is seen in a large percentage of the preparations.

Eleventh day. When lying on left side responded to stimulations such as twisting of the ear, by kicking and some slight movement of the head. Rigidity intermittent and less marked than before.

Twelfth day. When being turned on the mattress kicks vigorously. Taken out of the bath in the evening and dried preparatory to Physiological Society meeting at Oxford. During drying temperature fell to 36° C. and remained subnormal for several hours.

Thirteenth day. Weight when dry 2.45 kilos. Respiration rate 24. Reflexes very brisk as before and kicking movements when the animal is stimulated. During most of the time the animal did not have a typical extensor position but remained moderately rigid in a semi-flexed posture and with a rigid flexion of the ankle-joints of the fore limbs. Temperature fell again to 36° C. during the afternoon when exhibited at the Physiological Society. Replaced in bath in the evening. Animal had sores from friction under armpits and during replacing in the bath made inco-ordinated attempts to reach the sores with its head and hind limbs.

Fourteenth day. Respiration faster. Animal kicking a lot when touched.

Fifteenth day. Respiration 66. Reflexes very poor.

Sixteenth day. Respiration 44. Reflexes slightly better.

Seventeenth day. Respiration 32. Reflexes good, except for acoustic, which has been absent since the fourteenth day.

Twentieth day. Respiration 24. Acoustic reflex present again for the first time since pneumonia began. Fore limbs rigid, extended and without movements. Hind limbs have a curious slight walking movement even when animal is not touched.

Twenty-first day. Kicking movements when stimulated. Made occasionally a curious sound like an inco-ordinated mew.

Twenty-second day. Respiration 22. Pinna and corneal reflexes very brisk. Acoustic reflex good. Touching the face produces twitching of facial muscles, and even a slight movement of air across the face produces the twitching of muscles and shaking of the head. If animal is stimulated by twisting the ear curious walking movements occur, most marked in hind limbs, and sometimes accompanied by a curious crying sound.

Twenty-third day. Had caught fore-paw in thermo-regulator and had broken it. Animal found dead and temperature of bath 41° C. Death no doubt due to hyperpyrexia.

These two examples give a fairly good general impression of the results usually obtained, though there can be no doubt that the first of these showed some symptoms of raised intracranial pressure secondary to hæmorrhage and infection throughout its time of survival; it is probable that raised intracranial pressure caused absence of function of nervous centres close to the section, thus accounting for the sluggish reflexes and the relative simplicity of the reactions in the late stages compared with those shown by many animals.

(b) *Posture.*

The decerebrate rigidity remains as a general rule during the whole time the preparation survives, but after the first four or five days this position is less constant, and may alternate with others in which flexion, either flaccid or rigid, is conspicuous. At this later stage the variability of the positions assumed is noticeable, and it seems probable that the temporary disappearance of the rigidity is due to the assumption of other reflex positions. The maintenance of good rigidity over a long period, as in animal I, certainly makes it possible to exclude it being due to stimulation of cut nerve fibres, since these had undergone degeneration in this animal, and there is, therefore, good confirmation of the generally accepted view of the reflex origin of this position.

The rigidity shows variations according to the position of the animal, and to some extent these variations correspond with those described by Magnus and Kleijn and their co-workers [3], [26], [27], [28], [36], [37], [38], [39], [40], [61], but in the few animals that we have examined carefully we have been unable to get such consistent results as these authors have described. As in our animals the spinal cord has not been divided, the rigidity of the fore limbs is influenced by the position of the hind limbs, so that less constancy must be expected. In

general with the animal lying on one side all four limbs are held rigidly extended, but both the upper fore and hind limbs are relatively flaccid when compared with the lower. This difference is still observed if the animal is suspended in the air by holding it up by its skin while maintaining it in a similar position, but the difference in rigidity is less noticeable than it is when the animal is also receiving pressure stimuli by resting on the table. This contrast between the upper limbs and those resting on the table was very constant and was noticed in a large percentage of the animals, but even in this respect preparations are found in which this difference is scarcely noticeable, or in which the rigidity is asymmetrical so that the contrast cannot be observed. This asymmetry is especially apt to occur in the later stages when a position of general extension of the limbs is much less constant.

During the first few days the position usually assumed by a preparation lying on its side is that described already in the case of animal II on the ninth day, the position of the hind limbs being variable, though most commonly the upper hind limb was also held rather forwards and the lower farther back. On turning the animal over the limbs move, so that the same posture is assumed in the new position. This again is not regular; thus, for instance, in one of the earliest of these experiments, an animal (decerebrated June, 1914) maintained this posture constantly on whichever side it was lying, except on the second and seventh (the last) days, when the relative position of the limbs was the reverse of this, the lower fore limb being held forwards and the upper fore limb backwards. That this was a definite posture was demonstrated on turning the animal; then the limbs were moved so that this atypical posture was adopted also when lying on the other side. Such an atypical posture has sometimes been maintained by other preparations and has then been the usual position for that animal.

Rigid flexed positions may be assumed in an acute preparation, but under these conditions it is rare, and we have never been able to produce them, except accidentally; in the chronic preparations they are a comparatively common occurrence, and indeed some degree of flexion is usually found in one or more of the limbs after the first five to ten days, and, though it may alternate with extension, yet flexion may sometimes be the more constantly maintained posture. The most common of these flexed positions is a rigid semi-flexion of the fore limbs, or of one fore limb, with an acute rigid flexion of the ankle joints and extrusion of the claws of the fore limbs. The position is then one

similar to that assumed by a cat when holding a mouse in its claws or when climbing up a pole. An example of this will be seen in the case of animal VIII, of which a detailed description will be given later. A few other instances may be brought forward.

Animal III.—Large male After operation had rigidity of average intensity present in all four limbs; the rigidity was fairly symmetrical, though the head was held turned to the left. On the third day this rigidity became less noticeable and when turned the animal tended to curl up and flex the fore limbs. On the fourth day after turning, the previous degree of rigidity had returned, and was maintained on the fifth day. On the sixth day there was a rigid flexion of the ankle joint of the upper fore limb, on whichever side it was lying, with extrusion of the claws of this limb. On introducing a thermometer into the rectum both fore limbs were flexed with acute flexion of both ankle joints and extrusion of the claws, while several extensor thrusts were made with the hind limbs. In this animal the section passed through the anterior end of the right superior colliculus and through the middle of the left superior colliculus, to emerge ventrally 3 mm. in front of the pons at the level of the stalk of the pituitary, but no microscopical examination was made. This animal also gave pseudoaffective reflexes and will be referred to again later in this connection; the decerebration was by the older method in which all the brain above the section was removed so that there was no possibility of any connection with higher centres.

Animal IV.—Adult female. Post-mortem, see p. 250. Decerebrated by the later method, the rigidity was only moderate on the first day, but increased on the second, though still below the average, on the third day the animal kicked a good deal during turning, and then assumed a position of rigid flexion of the back and hind limbs with some flexion of fore limbs. On the fourth day there was an average rigidity in an extensor position, but flexion postures were assumed temporarily, during turning, &c., but were maintained only a few minutes, then gradually changing to an extensor posture. On the sixth day the animal was taken out and dried for examination in greater detail. On taking it out of the bath it went into a position of extreme extensor rigidity with retraction of the head. During drying with a towel it made many movements, kicking, withdrawing a limb that was being dried and shaking it, especially the left hind limb. It also made some progression movements. In between these movements positions either of rigid flexion or of rigid extension were assumed.

In the rigid flexed position the ankle joints of the fore limbs were acutely flexed and the claws extended. Unfortunately this animal vomited and choked during drying, so that no further examination was possible.

A position of flaccid flexion was also not uncommon in the later stages. An instance of this is described below.

Animal V.—Half-grown male. Post-mortem, see p. 250. Decerebrated by the later method. Three hours after operation showed little rigidity but made walking movements most of the time. For the first nine hours the animal was kept in an incubator but developed little rigidity; it was then put into a bath and on the next day the limbs had good extensor tone. On the third day there was little or no rigidity. On the fourth day rigidity was absent in the morning, the limbs being quite flaccid, but quite good rigidity developed on turning it to the other side. On the fifth day the rigidity was moderate and on the sixth it had again disappeared, though the pinna and other reflexes were good. The animal was then dried. On washing in alcohol and drying with a towel there were good movements of retraction with a shake of the paw of the limb being dried, especially in the fore limbs, and good extensor rigidity returned temporarily. When dry the animal appeared completely flaccid, with good pinna reflexes, shaking of the head on blowing in the ear, and retraction and shake of each limb on pinching. It was then given to Professor Sherrington for use in his experiments. As soon as dissection was started, kicking movements of all four limbs with movements of the head and neck were made, the animal micturated and then the preparation went into a posture of extreme extensor rigidity with considerable retraction of the head which it then maintained. Following this the extension became gradually less intense, though never disappearing entirely within at any rate twenty minutes, and was renewed in full intensity as soon as the preparation received further stimulation.

Other preparations were sometimes flexed and perhaps flaccid as they lay in the bath, but went into extensor rigidity immediately any examination was attempted. In one or two cases this passage from a flexed to an extended posture seemed to be induced by mere auditory stimuli, but no instance of this was seen in which the evidence was absolutely conclusive, owing to the difficulty of observing the animals while in a bath. It is conceivable that the flaccid flexion is a posture which has some relationship to the sleeping of a normal animal, but no proof of this is available.

Of the animals so far described two (animals II and III) have been distinguished by a tendency to turn their head to the left. This was a common occurrence, being noticed in fourteen animals as compared with nine that turned their heads to the right. This may have been due to the fact that the trephine opening was made on the left side and in consequence the section was generally a little oblique, and nearly always with the tendency to the removal of more on the left side. In thirteen of the above fourteen cases with head held to the left more brain matter was removed on the left side than on the right. On the other hand, of the nine preparations (see cats VI, VIII, XV,

XXII, XXIV), in which the head was held turned to the right, in four the section appeared to be evenly transverse, in four the section had the usual obliquity (more being removed on the left), but the turning of the head to the right was observed in spite of this; the level of the section was not determined in the ninth. The relationship is evidently complex, since the section had the usual obliquity in other cases without there being any asymmetry in the head position; undoubtedly during the first few hours stimulation may play a part.

In the one animal with more brain-stem removed on the right, which turned its head to the left, the position assumed may well have been due to stimulation, since it occurred during the first day, after which the animal died. Stimulation immediately after operation would also account for three out of the four cases in which turning the head to the right was noticed, although the section had removed more brain on the left side, since in these again the turning of the head was only noticed during the first day. In the animals with an apparently square section, in which the head was turned to the right, this posture was not marked except in one case. In all cases where there was an asymmetrical head position the level of the section was relatively anterior, and some few cells of the red nucleus were probably left intact and may have been functioning on one side at least. In fact, this whole turning of the head to the side most damaged might be explained if the tone of the muscles of the neck was increased by a crossed connection with a centre lying at about the level of the section, and it is possible that the lowermost cells of the red nucleus may function in this way.

Of the thirteen animals showing a persistent turning of the head to the left, one (XXVI) has been shown histologically to have had more of the red nucleus remaining on the right side than on the left, and in all the others the section was sufficiently high for a part of the red nucleus to remain, with the possible exception of two. The most difficult case to explain is that of animal VI (for post-mortem see p. 249) in which histological examination showed an almost complete destruction of the left red nucleus, the right red nucleus being partly present though showing some chromatolysis. Yet this animal gave auditory reflexes with movement of the head to the right during the two days it survived. Unless the hæmorrhage had interfered with the tract from the right red nucleus, the above hypothesis would seem untenable, and it cannot be regarded as established at present; further the posture is not

easily correlated with results of stimulation of the mid-brain reported by Graham Brown [8].

Many of the animals had sufficient rigidity to stand if propped into position, as described by Sherrington in the acute preparation, and most of them were able to maintain a very natural sitting posture. This consisted in making the animal lie on one side and propping up the body on the two elbows, so that the head was held in an erect position. Many could sit in this position on either side and maintain it for a considerable time, though usually after about five minutes the head would gradually drop, being allowed to fall sideways, and the preparation would lie down, the head in this procedure being carefully lowered so that no sudden impact with the table occurred. Similarly, the head was gently lowered if the animal was pushed over out of its sitting position. If the animal spontaneously held its head to one side, it was often only possible for it to balance itself in this sitting posture when lying on the flank opposite to the side to which the head was turned. All the postures assumed are more or less comparable with some seen in normal cats, the flexed positions that are often assumed in the later stages resembling those of cats curled up asleep.

(c) *Magnus Reflexes.*

These have been carefully investigated in two animals only owing to the difficulties with animals kept in a bath, though a few data resembling his results have been obtained on one or two other animals.

Animal VII.—Male, three-quarters grown. Post-mortem, see p. 251. Decerebrated by the later method. On examination twenty-seven hours after operation the animal could sit on either side and had good rigidity of all four limbs when standing, sitting, or lying on its right side. The rigidity of the fore limbs was less than that of the hind and was almost completely absent when the animal lay on its left side. In the standing position little change in rigidity was noticed as the result of raising or lowering head, and when lying on its back there was scarcely any rigidity in the fore limbs in any position of the head. When lying on right side bending the head down to the right increased the tone in the two hind limbs, and rotation of the head (jaw upwards) caused increased tone in the left fore and hind limbs and a slight decrease in the right hind limb, with no perceptible change in the right fore; the opposite changes occurred on turning or rotating the head in the opposite direction. Lying on the left side bending the head up to the right increased the tone in the right hind, but no other change was distinguishable, and rotation (jaw upwards) also increased the tone in the right hind, slightly increased that in the right fore, and slightly decreased that in the left hind; the opposite effects were obtained by the reverse movements.

Animal VIII.—Female. Post-mortem examination, see p. 252, and for more detailed description of the animal see p. 208. Decerebrated by the later method Examined on the seventh day. When lying on its back reflexes orthodox, showing flexion of the fore-limbs when the head was bent right forward, maximum rigidity with head in -45° or $+30^{\circ}$ position, this decreasing a little as the head was moved to 0° . This animal had little rigidity in the standing position and could not be made to stand. Placed on one side it assumed always a definite posture on whichever side it was lying; in this the lower fore was completely extended, the lower hind three-quarters extended, the upper hind semi-flexed and the upper fore was flexed and carried forward over the other, and the position of all the limbs was a rigid one. On flexion of the terminal joint of the upper fore there was extrusion of the claws. While lying on the left side bending head to the right caused extension of all limbs except that no change was noticed in the right fore; when on the right side there was extension of both fore-limbs and slight flexion of both hind on bending the head to the left. Lying on the left side, rotation of the jaw upwards caused extension of both hind-limbs and no perceptible change in the fore-limbs, on the right side rotation of the jaw upwards caused flexion of left hind and right fore, and extension of left fore, but no change in right hind. Movements of the head in the opposite directions in every case reversed the changes in the limbs, with the exception that rotating the head (jaw downwards) when the animal was lying on its right side not only reversed the changes in rigidity described for the opposite movement, but also caused a movement forward of the left fore-limb. In this cat the rigidity was slightly asymmetrical, since the preparation could sit on either side, but did so more evenly and securely if resting on its left flank, and it showed some tendency for the head to turn to the right. Some such asymmetry may account for the atypical reactions to these tests. The preparation died soon after the examination, apparently owing to a secondary hæmorrhage at the base of the brain.

(d) *Opisthotonos*.

This is not uncommon immediately after operation; in these animals the respiration rate is usually slow (though sometimes there is a fast and shallow respiration), and the condition is generally accompanied by tonic fits in which the rigidity undergoes extreme accentuation. In fact this head position was never seen except accompanying extreme extensor rigidity and merely appeared to be the result of such extreme rigidity. A few instances may be described.

Animal IX.—Old male. Post-mortem, see p. 247. Decerebrated (earlier method) 3.30 to 4.30 p.m. At 5.30 p.m. put into bath. Extreme rigidity, especially of hind-limbs.

Head retraction but not extreme. On second day reflexes brisk. Extreme rigidity of all four limbs. Lifts head to left to acoustic stimuli, but no

opisthotonos now seen. On ninth day extensor rigidity still good, having remained very marked since operation, but auditory reflex has almost disappeared since fifth day. Head retraction now again present. The rigidity of the hind-limbs is, however, definitely less than before, the fore-limbs are fairly rigidly extended except for a rigid flexion of the ankle joint with extension of the claws like that described in cat II. In the evening showed marked rigidity of mastication muscles with some clonus of the jaw on opening the mouth. Some nystagmus of eyes with rapid movement to the right, especially seen in the right eye. On the eleventh day found dead, and evidence found of old hæmatoma with later infection.

Animal X.—Decerebration (earlier method) 2.45 to 4.15 p.m. Considerable hæmorrhage. At 9 p.m. in incubator, rectal temperature $41^{\circ}2'$, respiration rate 24, rather irregular, and each inspiration accompanied by slight spasm of muscles of back. Rigidity intense and whenever the animal is touched it goes into extreme opisthotonos. At 10.45 p.m., temperature $38^{\circ}8'$, respiration rate still 24, with long inspiratory pause and only occasional spasm of back muscles. Attacks of opisthotonos as before. This opisthotonos was brought on most easily by touching the nose; it could be made to relax generally, but not always, by flexing the head, and would itself relax spontaneously to some extent after a time. On one occasion insertion of a thermometer into the rectum produced a strong defæcation reflex with immediate relaxation of the intense rigidity and disappearance of the opisthotonos.

On the following morning the opisthotonos had disappeared, breathing was more regular, 20 per minute, with a rectal temperature of $37^{\circ}8'$. Rigidity marked but not so intense, and twitching movements of all four paws present, these occurring with each inspiratory movement. On the third day respiration normal, muscle spasms no longer seen, and the animal made an inco-ordinated mew twice when taken out of the incubator. Animal died at the end of the day and post-mortem showed a considerable hæmatoma at the base of the skull. No detailed examination of the level of the section.

Animal XI.—Female, half-grown kitten. Decerebration (later method) 2.30 to 3.15 p.m. Signs of reactionary hæmorrhage immediately after operation with considerable oozing from the wound. Attacks of marked rigidity and head retraction. Found dead next morning. On autopsy considerable hæmatoma; the section extended from in front of superior colliculi to about 0.5 millimetres behind the anterior end of the pons.

It will be clear from these examples that this condition is seen in animals with evidence of post-operative hæmorrhage, and generally blood is also found below the tentorium. Death in the first twenty-four hours is common, but if the animal survives the opisthotonos disappears, and does not reappear again except in the case of an infection of the base of the skull such as was the case in animal IX. The exaggeration of the position as the result of some sensory stimuli, and

usually show either symptom, since it is careful to keep itself under comfortable conditions and has a thorough insulation in its fur. The metabolism of these preparations has not so far been investigated by us, but we have no reason to doubt the low metabolism figures obtained on the acute preparation by Roaf [47], since the difficulty of keeping the preparations warm has always been remarkable. The stretching out of the limbs in extension no doubt increases the heat loss, but even so it is surprising that keeping the animals on a warmed operation table, surrounding them with hot-water bottles and covering with a blanket, is usually only just able to keep the animal's temperature normal if the room is at all cold, i.e., 15° C. There is also some evidence that the metabolism is greater the higher the temperature and that it decreases with a fall in temperature, so that there is no effort at a control of body temperature through a control of metabolism. Thus in an incubator animal with its fur greased and in an atmosphere saturated with moisture (when the loss of heat is accomplished by radiation and conduction), the difference in temperature between the animal and the incubator is usually greater the higher the temperatures happen to be. Thus with a high rectal temperature a difference of 5° C. above the temperature of the incubator may be found, and with a low rectal temperature the difference between the two may be only 3° C. Thus there is a tendency for the rectal temperature to swing more widely than that of the incubator. The resulting difficulty in finding a correct setting for the incubator is readily seen by reference to a few examples.

The general correspondence between the animal's temperature and that of the incubator is well shown in fig. 1, which represents the temperatures observed in cat VII, of which some description has already been given. This animal was kept immediately after operation in an incubator in which the air was constantly saturated with moisture by having the wall covered with damped cloth. Considerable difficulty was found in getting a correct setting of the incubator and it is seen that between eight hours and twelve and a half hours on the first day the rectal temperature of the preparation dropped 2.1° C. (from 37.2° to 35.1° C.), corresponding with a fall of 1.5° C. in that of the incubator. It is also noticeable that after three and a half hours on the first afternoon the rectal temperature was 39° C. and was rising rapidly as the result of an incubator temperature of 29.7° C. dry and 29° C. wet bulb, while twenty-seven hours after operation the rectal temperature was fairly steady at only 36.2° C., though the incubator setting had now been adjusted to give a temperature of 30.3° C. dry and 29.8° C. wet bulb. The

difference in the two results is probably due to the gradual loss of the insulating action of the fur as the effect of the penetration of the moisture through it. This was demonstrated accidentally on the second afternoon. At 3.10 p.m. the animal was taken out of the incubator and was examined for Magnus reflexes in front of a gas stove until 4.25 p.m. During this examination its rectal temperature rose to 39.7°C , its fur became dry and in good condition, and it was then returned to the incubator in the belief that its temperature would gradually drop again to 36.2°C ., since the incubator setting had not been altered. The

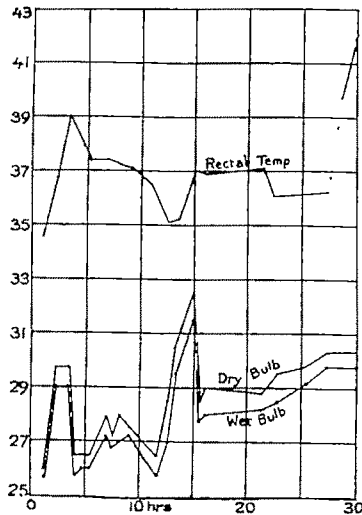


FIG. 1.—Experiment VII. Abscissa: Time in hours from end of operation. Ordinate: Temperature degrees centigrade. Lowest curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Upper curve: Rectal temperature of animal. Dotted part of curve: Change when animal was out of incubator being examined in front of a gas stove.

observer was interrupted by teaching work and when the animal was again examined, one hour and thirty-five minutes later, it was found to be dead, with a post-mortem rectal temperature of 42.1°C . This case, therefore, illustrates very well the difficulties of incubator preservation of these preparations, and the numerous factors that have to be taken into consideration, as well as demonstrating the absence of any control

The same points, and also the general course of such an incubator experiment, may be seen in the case of cat VIII (also previously described in relation to the Magnus reflexes). The general history of its temperature changes is illustrated in fig. 2; but a more or less detailed account may also be given to serve as an example of an incubator experiment.

Animal VIII.—Female. (For post-mortem see p. 252, and previous description p. 203). Decerebrated by later method so as to preserve stalk of pituitary. Rather ragged section and considerable hæmorrhage afterwards. Large piece of gauze left in, but in spite of this a considerable hæmatoma formed shortly after the end of the operation. Placed in steam-heated incubator at 30.8° dry and 30° C. wet, i.e., about temperature at which cat VII had a rapid rise of temperature on its first day. At three and a quarter hours the rectal temperature was still below 35° C.; at four and a quarter hours it was still only 34° C., though the incubator temperature had been still further raised. The incubator was then set to give 33.5° dry and 32.8° wet bulb, and the rectal temperature gradually rose to reach 38° C. after about nine hours. The

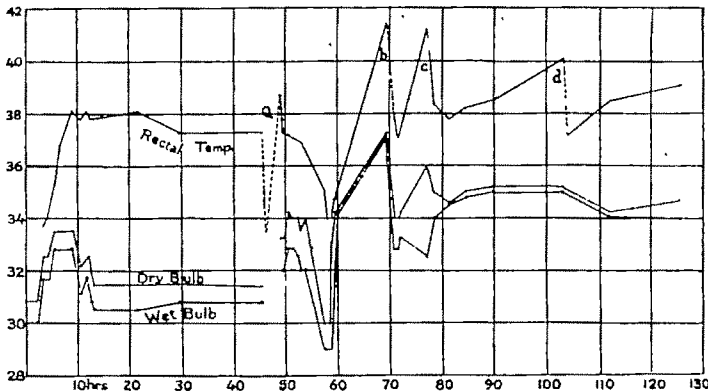


FIG. 2.—Experiment VIII. Abscissa: Time in hours from end of operation. Ordinate: Temperature. Lowest curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Top curve: Rectal temperature of animal. Dotted parts of curve: Animal out of incubator—(a) taken out, wound dressed; as bodily temperature fell fur treated with paraffin and animal then warmed in front of gas stove; (b) and (c) cooled by being kept in a room for a short while, (d) examined in front of stove for Magnus reflexes.

incubator temperature was then gradually reduced and regulated to give a temperature of about 31.5° dry and 30.5° wet bulb, when the rectal temperature reached a steady level at about 37.3° C. During this time the animal had had good rigidity of all limbs; twelve hours after operation it showed brisk corneal and pinna reflexes, and some mastication reflex, and when the ear was twisted it moved its head and fore limbs slightly and showed a definite increase in decerebrate rigidity.

Thirty hours after operation reflexes as before but mastication no longer seen; respiration rate 21, temperature 37.3° C. Lying on right side it now had good rigidity of all four limbs, but on turning on to left side showed some flexion of back, good rigidity of hind limbs, little rigidity in the left fore, and it held the right fore rigid, but flexed and placed forward across the left, with the ankle joint acutely flexed and the claws extended. It kept its head turned to

the right if put into a sitting posture. The tail was intensely rigid, and was wagged whenever the animal was touched.

Forty-six hours after operation taken out of incubator, and gauze plug removed from wound, hæmatoma found infected. Animal kept on warmed table but room temperature only 9°C . (owing to post-war conditions), and the rectal temperature soon dropped to below 35°C . Animal then warmed in front of gas stove and lubricating oil rubbed into fur to diminish its heat insulation value.

Returned to incubator at 2 p.m. (i.e., fifty hours after operation) with temperature of 38.7°C . The respiration rate was then 20, having dropped to 15 per minute when the body temperature was at its lowest. Fig. 2 shows the changes in temperature occurring after this and the close correspondence between the rectal and incubator temperatures. When the rectal temperature had risen to 41.6°C . the respiratory rate was 40, dropping again to a rate of 31 when the rectal temperature had reached 38.1°C . on taking the animal out of the incubator and keeping in a cold room. This drop of temperature occurred in about thirty-eight minutes, and yet there was never any sign of shivering. The posture of the animal when lying on the left and right sides was as before. The wound was opened up and some pus evacuated.

Sixty-six hours after operation the animal was again examined. It now had good extensor rigidity of all four limbs when lying on the *left* side, and on being turned to the *right* side there was good rigidity of the hind limbs and extrusion of claws, and on stimulating by twisting the ear the fore limbs assumed a rigid flexed position with extrusion of the claws, and maintained it.

One hundred and three hours after operation the rectal temperature was 38.5°C ., and the respiratory rate 32. The upper fore limb was kept flexed on whichever side it was lying. On touching the animal there was reflex extrusion of claws and either retraction or prodding forward of the limbs.

One hundred and eighteen hours after operation the animal was much as above, but when traction was made on its flexed upper fore limb, it withdrew it with a clawing movement. It also made a cry—an inco-ordinated mew—when being turned.

One hundred and twenty-seven hours after operation was as above but on various stimuli, such as mere touching, would often extend a limb and spread out claws, in the position a cat holds its limbs when stretching after waking up.

At the end of the sixth day the position of the animal on whichever side it was lying was very definite and has already been described in connection with the Magnus reflexes. It had no auditory reflexes, but by this time some mastication had again returned. The respiration rate was 33 with a rectal temperature of 39.1°C . There was a discharge of pus and wax with disintegrating hæmatoma from the wound, and in the middle of the seventh day the animal died as the result of a secondary hæmorrhage within the cranium. Urine passed during the third day contained no trace of sugar.

The effect of body temperature on the respiratory rate is also well shown in the case of cat XII kept in an incubator with a wet bulb control, but in which the air was not saturated with moisture and where the insulating action of the fur was not interfered with. The changes in body temperature and of the incubator for thirty hours, starting seven hours after the end of the operation, are shown in fig. 3; the wet and dry bulb readings were taken at frequent intervals and the rectal temperatures were taken with an electrical resistance thermometer and were recorded every minute on a Gamgee [16] thread recorder as

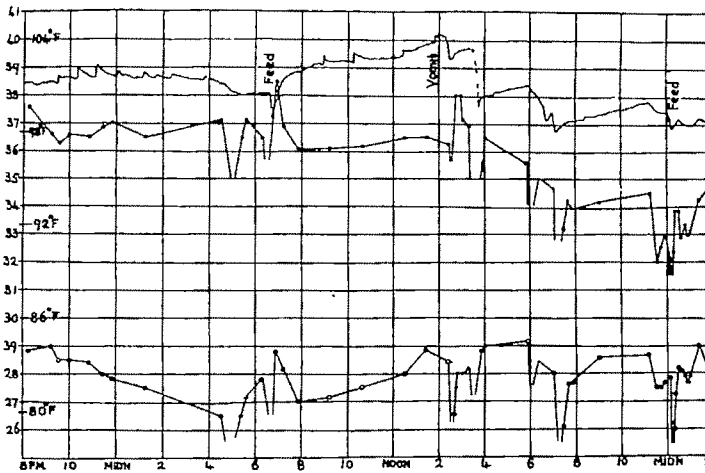


FIG. 3.—Experiment XII. Abscissa: Time. operation finished seven hours previous to commencement of record. Ordinate: Temperature. Lower curve: Wet bulb temperature of incubator. Middle curve: Dry bulb temperature of incubator. Upper curve: Rectal temperature of animal (record with resistance thermometer). Gaps in records, opening of incubator door.

described by Woodhead and Varrier Jones [65]. In all, more than forty-five observations of the respiratory rate at varying body temperatures were made on this animal, though the results were somewhat modified by the gradual development of mucus in the trachea giving some irregularity in the respiration with a later development of lung congestion. If all the figures for the respiratory rate during the first few days are averaged the following results are obtained:—

Temperature		Number of observations	Average rate per minute
36° to 37°		4	23
37° to 38°		18	28
38° to 39°		16	33
39° to 40.1°		7	36

If, however, only the earlier figures are taken, before much tracheitis had occurred, the respiratory rates are rather slower but the relative differences are much the same.

Average temperature			Number of observations			Average rate per minute	
36.1°	..	..	..	1	..	..	15
37.2°	..	..	..	4	..	..	19
37.8°	..	..	..	5	..	..	25
38.0°	..	..	..	2	..	..	29
38.3°	..	..	..	4	..	..	31
38.7°	..	..	..	4	..	..	32
39.5°	..	..	..	3	..	..	38

The brain section in this animal was from the anterior end of the inferior colliculi to 1 mm. in front of the pons, but a detailed histological examination was not made. It will be noticed that in this

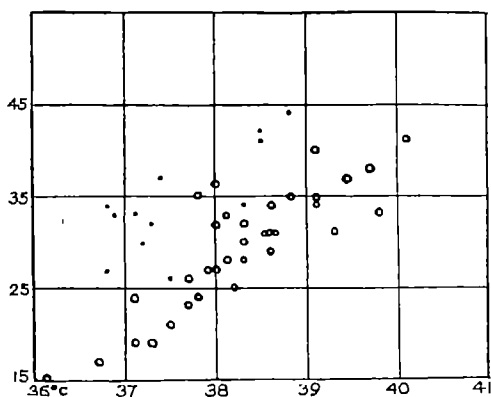


FIG. 4.—Experiment XII. Abscissa. Rectal temperature. Ordinate: Respiratory rate per minute. Variations in respiratory rate with changes in temperature. o = Observations during first twenty-nine hours. . = Observations made later than this.

animal as well as in cat VII there was a very definite dependence of the respiratory rate on the body temperature. This is still more clearly seen in fig. 4 in which the respiratory rate observations are plotted against the body temperatures. The figures are obviously affected by other factors, such as the mucus already referred to, and quite possibly the respiratory rate is different for any given temperature, if the temperature is then falling, compared to what it would be if the temperature were rising. In spite of these variable factors it is clear from a consideration of these two examples that there is a relationship, and that the temperature coefficient is rather high, probably about 4.0, possibly as high as 5. But in any case the effect is much less than in the normal cat where a slight rise in body temperature may easily

give a respiratory rate of 80 [20] [30] [48]. That the temperature coefficient is so high may be partly due to the fact that not only might the change in temperature affect the respiratory centre directly, but it might also do so indirectly through altering the metabolism.

In only one instance was a really fast respiration seen with a raised body temperature. In this animal the temperature rose to 42.8° C. in an incubator through an accident. At the time of observation it was moribund and its respiratory rate was about 60, but this animal had had a considerable reactionary hæmorrhage, with marked opisthotonos and convulsive spasms, and its fast respiratory rate may have been due to other factors. In any case the rate observed is not very different from what might be expected at this body temperature, judging by the other animals. The section in this animal was also rather anterior and very ragged.

With regard to the respiration it should be noted that as a rule with a normal body temperature the respiratory rate was about 24 per minute, which is about the normal rate for a cat. Irregular and spasmodic breathing described by Macleod [34] [35] as occurring spontaneously in some animals after decerebration was not seen except where there was fairly definite evidence of hæmorrhage, as in cat X, nor can we agree with the provisional statement made by Macleod that "when the posterior corpora quadrigemina are even slightly wounded spontaneous respiration is seldom, if ever, observed." We have repeatedly made sections through this level and observed normal respirations, and we have even made sections through the very posterior edge of the inferior colliculi without having trouble with the respiration (e.g., cat XXI described later, survived over twenty-two days with a normal respiratory rate, and cats XX and XXIII furnished other examples of this). The contrast between our experience and that of Dr. Macleod may depend on the fact that our animals immediately after the operation were left quite quiet without further experimentation, while such a course is impossible in dealing with the acute preparation. Any manipulation or stimulus must increase the risk of reactionary hæmorrhage either below the tentorium or into the substance of the medulla, and that this was a common occurrence even in our animals may be seen by reference to the anatomical descriptions. Clearly the macroscopical inspection of the brain-stem does not allow the physiological level of the decerebration to be determined, and consequently discrepancies between different observers are to be expected according to the relative probability of post-operative hæmorrhage. A similar

explanation may well account for the discrepancies between Trevan [58] and ourselves as to the effect on the respiratory rate of section at various levels.

Fig. 3 demonstrates well how sensitive the body temperature was to the changes in the incubator produced by opening the door for a few minutes, as for instance for feeding

That the wet bulb temperature is very important is shown by the fact that animal VII required a wet bulb temperature of about 29° C. with a dry bulb reading of about 30° to maintain a normal temperature, while animal XII required a wet bulb temperature of between 28° and 29° with a dry bulb of about 34° for the same result. And yet it was not the only factor; the rectal temperature showed a rise in cat XII between 8 a.m. and 2 p.m. with a rise in the wet bulb temperature, but it also showed a fall between 4 p.m. and 10 p.m. although the incubator wet bulb temperature had altered very little, while the dry bulb fell considerably. Also the difference seen between animals VII and VIII, one requiring a wet bulb temperature of 29° and the other of 31° (before the fur was greased) with almost complete saturation with moisture, to maintain normal conditions, requires explanation. Cat VII had an excellent coat and cat VIII was rather mangy, and this may well have been the cause.

The incubator temperatures in the case of cat XII were rather variable; the reason for this was that the outer door of the incubator was left open throughout the experiment to allow the repeated examinations of the respiratory rate on this animal, and the glass door did not give adequate insulation. The sudden peaks occurring in the rectal temperature record in this figure are also of interest. They were always seen when an animal attempted to defæcate against the resistance of the thermometer; since they show fairly steep falls directly the efforts ceased they may represent a change in temperature which was chiefly local.

The absence of shivering on cooling was specially tested in one animal (cat XIII) four hours after operation. This animal's reflexes were brisk and the section was an anterior one passing through the superior colliculi to 2 mm. in front of the pons; it was operated on by the older method. Though its temperature was reduced from 39.5° to 37.8° by wetting with cold water (the normal temperature for a cat is about 38.5°) within five minutes, yet no sign of shivering was seen. In another animal which has already been referred to (cat V) the preparation was kept in an incubator for the first nine hours; it was con-

stantly making running movements, so that it was not found easy to balance the heat exchange. At the end of this nine-hour period its rectal temperature was 40.9°C .; then it was cooled down by holding under a tap delivering water at 16.5°C ., the water being rubbed into the flanks, so that the temperature fell to 37.8° within sixteen minutes, and yet no sign of shivering could be observed. That shivering does not occur either even in animals that have survived much longer is clear in that no such movement was ever seen in animals, such as cat II which was taken from a bath and had its temperature dropped rapidly from a normal level to one much below normal during the process of drying.

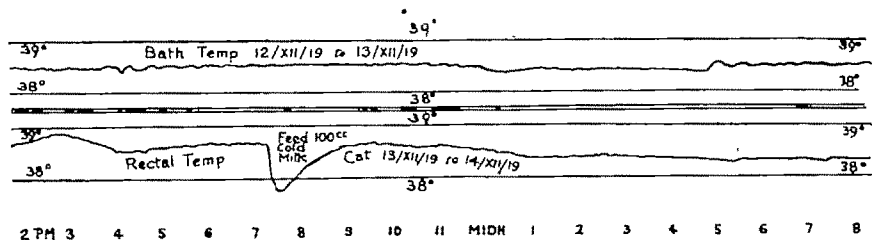


FIG. 5—Experiment XIV. Abscissa: Time. Ordinate. Temperature. Lower curve: Rectal temperature of animal in bath, December 13 to 14. Upper curve: Temperature record of bath December 12 to 13.

Fig. 5 gives examples of records with a resistance thermometer of the rectal temperature of animal XIV (described a little later) kept in a water bath, as well as a record of the bath itself, the two records being taken on successive days, and the part reproduced includes the early morning hours when the greatest fluctuations of the bath temperature usually took place. The relative steadiness of the rectal temperature by the use of this method is very noticeable, and also the rapid drop of nearly 1°C . in the rectal temperature on feeding this animal (of 2.1 kilo weight) with about 90 c.c. of cold milk by stomach tube. The effect of feeding was always marked, if the food were cold, so that in incubator experiments it was necessary first to warm the milk to the body temperature, since under these conditions recovery of a normal temperature took place much more slowly.

(f) *Pseud affective Reflexes; Mastication and Vocalization.*

Pseud affective reflexes have already been described by Woodworth and Sherrington [66] in acute preparations, and all those that they have described may be observed in the chronic animal, as well as others which are rarely seen except after survival for a few days. The most

common of these reflexes is the lashing of the tail when the animal is touched or stimulated, as by twisting the ear; this reflex is seen in a large percentage of the preparations (both acute and chronic), e.g., cat VIII. Kicking movements and running reflexes may also be induced often by touching an animal, as happened for instance in animals II, IV and V. All these reflexes may be seen in the acute preparation, but they become more common as an animal is kept, and may often be present after the fourth day when the animal has been entirely passive during the first few days. The kicking movements are usually more widespread and general in the later stages than in the earlier, and while they are relatively difficult to induce in the first few days except by strong stimulation of some area on the head, in the later stages mere touch stimuli at any situation will often produce a reaction. Some instances of these may be briefly described.

Animal XIV.—Female. Decerebrated by earlier technique. Had good rigidity with head held to the left, brisk pinna and conjunctival reflexes. pricking of the left ear to auditory stimuli, and it swallowed a stomach tube with a passive reflex action on the first day. By the fourth day the head was raised to the left when sounds were made, especially to such noises as shuffling the feet on the floor, and the stomach tube was only swallowed after apparent objection. This consisted in bending the head backwards, biting, attempts at spitting out the tube and general movements of the head which suggested an attempt to get rid of the tube. The eyes had been washed out with water every day, and on this day it began to "object" to this process, squirming its head backwards and making the washing difficult. On the fifth day there was some conjunctivitis of the left eye and the washing of the eyes was also accompanied by movements of the legs. The section passed just in front of inferior colliculi dorsally to about 3 mm. in front of the pons ventrally. No detailed examination was made.

Animal XV.—Male Decerebrated by later method. Rigidity good and reflexes good. Slight movements of progression in left hind limb on first day. On second day some progression movements, though slight, in all four limbs from time to time. Stomach tube swallowed passively. No auditory reflex.

On third day on turning the cat over, it had a flexion spasm of both fore paws associated with an increased rate of respiration and some turning of the head to the right.

On fourth day some chewing of the stomach tube but no "objection" to it. A slight nose-licking reflex present after feeding.

On fifth day there was some conjunctivitis. On cleansing the eyes there was apparent objection, movement away of the head and bringing forward of the fore paws as though to push the hand away, but this was badly co-ordinated and ineffective. The condition remained much the same till the eighth day.

when the animal "jumped" and showed increase of rigidity on cleansing the eyes but no longer moved the fore limbs. It died from a septic enteritis and pneumonia at the end of the eighth day. The level of the section was symmetrical and passed between the colliculi dorsally to the anterior edge of the pons.

These animals illustrate the gradual change during the first few days with the appearance of reactions not seen at first. Ophthalmia was a common occurrence (due no doubt to their blindness); the apparent objection to the cleansing of the eyes was never seen in the first few days, but was nearly always seen after the fourth or fifth day. During the first few days after operation, the stomach tube is usually well swallowed but without any effort at mastication, after this there is often developed a more complicated reflex, in which the tube is taken with avidity with a well co-ordinated chewing movement which might be so effective as to puncture a stout rubber catheter. Once the tube had reached the stomach the chewing movements would usually cease, to recur again from time to time. It was often noticed that these chewing movements recurred more commonly at a time when milk was flowing through the tube into the stomach. Whether there was any reflex connection between the stomach distension and the mastication reflex is however doubtful, since at this time mechanical movements of the tube in the mouth were liable to occur. On the removal of the tube in a good animal there would occur a nose and mouth licking reflex, usually continuing for two or three licks. A similar nose licking reflex has been described in dogs by Meltzer and Githens [42], and like them we have found that such a response may sometimes be induced by pinching of the nasal septum, but in our preparations it occurs much more regularly as a part of a mastication complex. This nose licking is also very common, even in animals that do not otherwise show it, just before vomiting occurs, and under these conditions some mastication movements usually accompany it.

The mastication movements were usually well co-ordinated and after a few bites food placed near the back of the mouth was swallowed, but the mastication was never sufficient to bite any solid food into small fragments; if the solid food were placed in the front of the mouth it might remain there without any movement occurring, or it might be spat out, or very occasionally chewing movements might be induced. If a number of pieces of solid food were given to such an animal the reflex soon fatigued (a cat is a slow eater) and the bolus of food was left stationary, even though lying at the back of the throat. If such a pre-

paration was then stimulated, as for instance by a slight tap on the nose, it would shake its head, apparently "wake up" and the bolus was immediately swallowed. A mastication reflex was often induced by merely opening the mouth. The position of the section in animals with simple mastication reflexes may be seen by reference to cats III, IV, VIII, all of which showed this reflex well.

After the fifth or sixth day pseudoaffective characteristics often appear in this mastication reflex, the tube being apparently objected to as in animal XIV, though food would be well taken. In this reaction it may kick and bite and make the other movements described in the case of cat XIV, or it may be less definite. The sequence of different types of mastication reflex is usually as above, but there are variations, and in our series of 124 complete decerebrations we have had two which showed this seeming objection even on the first day. This was the case with animal XII already referred to, and also in the case of a kitten of 1.7 kilo weight (cat XVI) in which the section passed between the colliculi to the anterior end of the pons. It will be noticed therefore that in these cases the sections were at a normal level.

In many cases the mouths of the animals were washed with 1 in 60 carbolic for cleansing purposes. This process has also been accompanied by a seeming objection, shaking of the head, movements of the limbs, &c.; this reflex also has not been seen during the first few days.

Though the reflexes so far described seem superficially to have some relationship to emotion, they are clearly, even to a casual observer, merely pseudoaffective, since they differ from many spinal reflexes only by being rather more elaborate, and since in such a decerebrate animal they appear with a mechanical precision whenever the animal is put under the same conditions. It is also very noticeable that a preparation that appears to object strongly to having its eyes washed will allow the wound on its head to be picked up roughly with forceps while a stitch is passed or removed, and not a movement of its limbs may occur, though a simple rigid extension is maintained. To the stimulus of a foreign body in the eye it has an habitual reflex response, but the puncture of a needle in the scalp is an abnormal stimulus unconnected with any habit or reflex. We can therefore unhesitatingly confirm Sherrington's interpretation of these phenomena.

A type of pseudoaffective reflex very rarely seen except in chronic preparations is vocalization. This was only seen in a small percentage of the animals, occurring in ten out of the series of 124 operated on

Of these ten animals four purred, and where purring occurred at all it was usually repeated. An example is described below.

Animal XVII.—Male kitten, weight 1'3 kilo. Post-mortem see p 248. Decerebrated by earlier technique. Reflexes fairly brisk and moderate rigidity on second day. On fourth day purred after feeding. This commenced about five minutes after the end of feeding and would then continue for a considerable time. Purred after each feed till the sixth day. When touched would stretch out claws. Occasionally spontaneous purring occurred in bath. On sixth day head wound suppurating and purring reflex no longer seen. On seventh day reflexes very sluggish, even swallowing reflex being poor. Stomach tube inserted in consequence into trachea and 70 c.c. of milk poured into it. (In the ordinary reflex animal it is practically impossible to put the tube down the trachea owing to the swallowing reflexes.) Considerable dyspnoea after this. When fed again, eight hours later, reflexes still very bad, but on stroking the chin after feeding it commenced to purr, but this only lasted about a minute. On ninth day the wound suppuration was improving and reflexes much more brisk. Purring again after morning feed. On tenth day reflexes very dull, respiratory rate very fast and no purring. Death later in the day from lung abscess and empyema, obviously resulting from the passage of milk into the lung.

Animal XVIII.—Young female, weight 2 kilos. Decerebrated by earlier method. Auditory reflex and purring after food present on first day. Vomited and died of suffocation on first night. Section through anterior part of inferior colliculi.

The occurrence of purring with regularity after feeding was very striking and it could not be induced in any animals in any other way. Possibly on the seventh day in cat XVII the stroking under the chin assisted in the development of the response, but it is unlikely, since this form of stimulus was often tried and never at any other time with success. On the other hand, food in the stomach formed the stimulus for the purring in three out of the four animals; the fourth in which it developed spontaneously will be described in more detail later. The disappearance of the purring after food in cat XVII with the development of suppuration in the wound, its return as the wound condition improved, and its disappearance again with the development of the lung abscess was very noticeable, and is of interest in that the animal was kept in a bath, so that the body temperature remained fairly constant, except that the animal was once taken out and dried in an incubator. Purring was observed with a rectal temperature as high as 39.2° C. in the bath and as low as 36.5° in the incubator, while the temperature during the time that purring was absent was about

39.2°, so that it was not change of temperature that caused the purring to cease. With infection, however, there is evidence of the dulling of this reflex, much as infection will diminish spinal reflexes in man or decrease the appetite. But the condition in these preparations is very different from real appetite, since though the purring occurs after food, no sign of even a pseudoaffective response is observed if food is withheld.

Animal XIX.—Young, weight 2 kilos, sex not noted. Decerebrated by earlier technique. After operation had good rigidity, good reflexes, head kept to left. Maintenance of good sitting posture lying on right side. No auditory reflex. One and a half hours after operation put into bath and showed repeated strong movements of head to left resembling a clonic movement. After two and a half hours found in bath clawing at the stirrer, all claws extruded but animal purring. On handling it made violent kicking and running movements, and in this kicking its head fell under water. After this it gave two loud co-ordinated mews—not those of pain so much as those of an angry cat. It was taken out of the bath and wrapped in a towel, when it purred again for a while. It was then put back into the bath, when it had no further movements but commenced to purr again. Reflexes and rigidity good. Slight movements of head to acoustic stimuli now present. Later it commenced kicking movements again, but was hobbled. Sounds appeared to increase the movements. When fed it swallowed the tube normally and no purring was noticed after. The wound was restitched with no reaction by the animal occurring. It died during the night, possibly from hyperpyrexia as the result of violent exercise in the hot bath.

Autopsy showed a slight intracranial hæmorrhage (about the size of a small pea) and the section passing through the anterior half of the superior colliculi to 2 mm. in front of the pons, the section being slightly oblique with rather more removed on the left than on the right. All the nervous tissue above had been completely removed. Histological examination was not possible owing to post-mortem softening.

This animal appeared to have vocalization reflexes occurring immediately after operation in a more or less disorganized form. It will be evident from the three examples quoted that the level of the section has been rather anterior, and it might have been concluded that the reaction depended on centres lying above the level of the pons. But another cat which purred (cat XX) seems to disprove this.

Animal XX.—Female, weight 2 kilos. Decerebrated by earlier technique. Rigidity good. No auditory reflex. Purred after feeding on the third day, and repeated this after all meals until it died at the beginning of the fifth day. Cause of death uncertain, though there was superficial infection of the wound.

The section passed through the lower parts of the inferior colliculi to the upper edge of the pons. No histological examination attempted owing to post-mortem softening of the brain.

It seems to be therefore established that purring reflexes depend on reflexes through centres in the medulla—though such centres are probably high in the medulla, since the reaction is usually not seen for the first few days after operation, and shock is probably more prolonged in the immediate neighbourhood of the section. It is noticeable that purring was only seen in young animals, and then usually in females, all animals which might be expected to purr readily during life, and in which there may have been a purring habit. The possibility of a medulla-initiated habit is strengthened by a consideration of those animals in which vocalization in the form of growling occurred.

Growling was observed in three animals, and shows considerable contrasts when compared with the purring reflexes. All three animals were adult males, and two of them old scarred animals which had evidently done a lot of fighting. The sound was exactly that made by a cat when fighting, and none of the animals made the sound more than once. In one case it was made on the fourth day when the animal's mouth was being cleaned with carbolic, in another (cat XXI—for description see page 221), about two hours after operation as a reaction to air blown into its ear; and in the third (cat III already described) it occurred about three hours after the operation, when the animal was put into the bath. None of the animals repeated the sound (even though cat XXI survived for twenty-two days), however much they were subjected to noxious stimuli.

Here, again, the vocalization was of a type suggesting that habit formed an important factor, but in this case the sound occurred as an isolated phenomenon, and was not repeated in a reflex and automatic manner as was purring.

Cat III was peculiar in that it gave this growling sound on the first day and no more sounds till the sixth day, when it made a sound somewhere between a growl and a mew while having its temperature taken with a rectal thermometer, at the same time making kicking movements which have been described already. The insertion of a rectal thermometer was an occurrence which was often repeated, and yet only evoked this reaction once, and the same animal on the seventh day gave a series of ten loud and well co-ordinated mews when being turned on its mattress—another response which it could never be persuaded to

repeat. At the end of the seventh day it died—the exact cause being uncertain.

An indefinite cry somewhat similar to a mew has been observed in five animals, of which cats II, III, X and XXI, supply instances. In the other instance the sound occurred once on putting the animal into the bath on the first day; in this animal the section was anterior, from the anterior end of the colliculi to 1.5 mm. in front of the pons, though operated on by the later method. In the case of this sound repetition was occasionally seen, but it could never be reproduced consistently as could purring. This cry is probably similar to the cry made by an animal under an anæsthetic, and which Sherrington [55] [66] has described as occurring also in decerebrate animals while anæsthetized. A normal mew was only observed twice—in cat III, as described above, and in cat XIX, of which details have been already given. In neither case was the mewing repeated, nor could it be produced by subjecting the preparations to nocuous stimuli.

One preparation must now be briefly described to give a clearer picture of the mode of occurrence of pseudoaffective responses in general:—

Animal XXI.—Long-haired male; weight 2.5 kilos (For post-mortem see p. 246). Decerebrated by older method. Had good rigidity one hour after operation, but no good sitting posture adopted. No movements made. Head kept to the left. On putting into bath two hours after operation and blowing into ear when it lay on right side, left pinna retracted, head raised to left and slight low growling sound made. On third day rigidity good, some doubtful pricking of ears to sounds. On fourth day began to kick a lot when turned. On sixth day respiratory rate irregular—about 30 per minute—quickenings when the animal was touched. For the first time showed apparent objection to swallowing of stomach tube. On eighth day apparent objection to cleansing of eyes and mouth. Considerable kicking movements when turned, running movements when rectal thermometer inserted. While having eyes cleansed twice made an indefinite cry. Mastication reflexes good—chewed and swallowed piece of meat put into very front of mouth, but on repeating spat second piece out. On twelfth day made movements of resistance against any interference with the position of its head. On thirteenth day respiratory rate raised after turning (apparently as the result of reaction to handling) to 36, to drop to 24 on leaving the preparation undisturbed.

The condition remained as above, but without any more sounds being made till the beginning of the twenty-second day, when the rigidity became less and the reflexes duller, the animal dying at the end of the day.

(g) Spontaneous Movements.

Spontaneous movements in the form of progression as well as movements of the pseudoaffective and defence type have already been described, and it is clear that a distinction must be drawn between the progression movements and pseudoaffective responses found after a section through the inferior colliculi to just in front of the pons and those seen when the section was 1 to 3 mm. more anterior, especially on the ventral aspect of the brain-stem. In the former, the pseudoaffective responses usually developed only after two to four days, and though they gradually became more active (e.g., cat II), they were never violent. In the latter (as in cat XIX) these movements were seen soon after operation and were much more violent.

Nothing can be added to the description of this second type of animal already given by Woodworth and Sherrington, except to draw attention to the exceptional case with vocalization (cat XIX) already described, and to note that on two occasions such animals have raised themselves from a lying to a standing posture in the incubator and have been found leaning upright against the side of the incubator. Three animals may be briefly described.

Animal XXII.—Female. Decerebrated by older technique. Nystagmus to right and jerky movements of head to right immediately after operation. One hour later found standing in incubator, leaning against side and attempting progression. It died shortly after this. The section was anterior to the superior colliculi and 7 mm. above the pons ventrally with many small punctate hemorrhages in the mid-brain above the level of the middle of the posterior colliculi. There was a considerable amount of blood-clot lying around the cerebellum and medulla.

With this animal may be compared another (XXIII) in which the section, though low posteriorly, was anterior on the ventral aspect, and one (XXIV) anterior both on the dorsal and ventral aspects.

Animal XXIII.—Adult male. Post-mortem, see p. 248, and figs. 22 and 23. Decerebrated by older technique. Rigidity good. On second day on cleansing the mouth with carbolic it kicked violently and moved about a great deal. The respiratory rate remained about 19 to 28 during "life"; it was constantly making progression movements spontaneously, but only kicked violently when touched. Died on sixth day.

Animal XXIV.—Female. Decerebrated by older technique. Three-quarters of an hour after operation found standing in incubator leaning against the side with its head down biting the wire netting floor. It was making violent kicking movements. It was taken out of incubator and then remained quiet.

but showed auditory reflexes. After another forty-five minutes it was put into the bath, when it again had a paroxysm of most violent movements. It died about four hours after operation. The section passed through the superior colliculi and was 4 to 6 mm. in front of the pons ventrally. There were three small punctate hæmorrhages in the mid-brain just below the posterior colliculi and considerable subtentorial hæmorrhage extending around the cerebellum and medulla and some way down the cord.

The movements in these anterior sections recur in paroxysms every fifteen to forty-five minutes, the intervals being shortened if the animals are exposed to stimuli such as touches, shakes or sounds. On the other hand, immediately after such a paroxysm there is a refractory quiescent interval, and in such an interval an animal of this type will lie quietly passive in a condition of simple decerebrate rigidity while a wound is stitched, although fifteen minutes later it may react with the utmost violence to a slight stimulus such as a jar or sound. Here, again, there is no evidence at all of any conscious sensation or emotion.

In these animals the movements usually resulted in reactionary hæmorrhage and it has never been found possible to preserve them for more than a few hours. A contributory factor to their death may well have been the respiratory irregularities described by Macleod [34], though in our animals movements were so active and general that it was not possible to judge whether there was any hyperpnœa other than that secondary to the exercise.

Slight vomiting just before death was in these a common occurrence.

Of other movements that have been observed two are worthy of notice. One has been described in cat II—an apparent attempt to reach a sore spot on its skin with its fore-paws, and the other was a complex scratch movement made by cat XIII, which four hours after operation curled itself up into a flexed position, although it had good extensor rigidity, and made (almost completely) the movement used by a cat when scratching the back of its neck with one of its hind limbs.

It is noticeable that violent movements and vocalization were only seen in one animal out of twenty-seven operated on by the later technique. In the latter technique the section had a different obliquity, passing usually from just in front of the corpora quadrigemina to just *below* the anterior border of the pons, and in the one exception where violent pseudoaffective movements were made soon after operation and where an indefinite cry was also made, the section had passed just in front of

the superior colliculi to 1.5 millimetres in front of the pons. The centres responsible for this reaction therefore probably lie nearer the ventral than the dorsal side of the brain-stem, since it is the level of the section on the ventral aspect that makes the most difference (contrast however cat XXIII). And yet the animals operated on by the later method showed the other more common pseudoaffective responses and were very hable to make progression movements, in spite of the different obliquity of the section.

(h) *Acoustic Reflexes.*

Acoustic reflexes have been described in the case of animal II and a similar lifting of the head to the left was also seen in cat III, commencing about two hours after operation, and some such reflex was also present in VI, IX, XIV, XVIII, XIX, XXI and XXIV of the animals so far described and also in animal XXVI to be described later. No doubt the other acoustic reflexes described by Forbes and Sherrington [14], such as wagging of the tail in response to high notes, may have occurred in many of the animals, but their position in the bath was not favourable to its observation and it was only noticed in a few animals. Movement of the head and of the fore-limbs was observed in many animals and was usually particularly noticeable, as in animal II, in those cases where the rigidity of the neck muscles was uneven so that the head tended to go to one side or the other. Apparently the stimulus increased the rigidity, and this being uneven, movement of the head resulted. In no case did an animal raise its head to sounds regardless of the position it was lying in; invariably the head was only moved to one side or the other.

The auditory reflexes became usually much more brisk after two or three days, and might often be seen at this stage when there had been no sign of them earlier, so that their absence could not be presumed unless the preparation had survived at least three or four days.

The greater reaction to high notes, resembling the roof-cries of cats, noticed by Forbes and Sherrington, was often confirmed; on the other hand, in many animals the most effective sound was a small scratching noise, and an animal would often react promptly by raising its head if a piece of paper was crumpled up at a distance of one or two yards. These sounds are similar to those made by a mouse. One reaction to sounds sometimes observed was the extrusion of the claws in the fore-limbs, which may perhaps be a guide to the nature of the reflex. Animals would react to these slight noises even though there was a

constant loud noise from the motor and stirrers, to which no reaction was shown except when it was started after an interval of rest. It is worth noting that in the older technique a reaction to sounds was noted in most animals where the section passed in front of the inferior colliculi to about 2 mm. in front of the pons, but even so not in all, and that it was seen in one in which the section commenced in the middle of the inferior colliculi and passed to the same level. It was never seen in sections by the later method with a different plane of section. If this passed from the anterior end of the superior colliculi to the anterior end of the pons, but was seen in one case where the section passed from just in front of the superior colliculi to 1.5 mm. in front of the pons, in the animal which has been referred to as having spontaneous violent movements and vocalization. It would appear therefore that here too the level of the section ventrally makes more difference than the level of the section dorsally, and that the highest link in the chain for this reflex may be nearer the ventral than the dorsal part of the brain-stem.

On the other hand, in cat XXIII (see figs. 22 and 23 and p. 248), no auditory reflex was observed, though the section was anterior on the ventral aspect.

(i) *Nystagnus*.

Spontaneous nystagnus was seen in several preparations, but usually in the first few hours only after operation, and probably as the result of irritative effects of hæmorrhage.

In animal XXII already described there was a jerky movement of the head to the right accompanied by nystagnus, which was kept up spontaneously during the few hours of life.

Two animals may be briefly described.

Animal XXV.—Adult male. Decerebrated by earlier method. Two and a-half hours after operation had extreme rigidity and made running movements when touched. Five hours after operation had paroxysms of violent fighting movements, claws extended, springing movements also made. General appearance of anger, but all movements inco-ordinate. Several paroxysms at about fifteen-minute intervals. Pinna reflexes brisk. No definite auditory reflexes. Just before the attacks there was some increase in the already very great rigidity, with some retraction of the head, which was also bent to the left. With this there was nystagnus to the left and jerky movements of the head to the left, present to a slight extent all the time, but exaggerated with the commencement of a paroxysm. Animal died in the night, vomiting slightly before death. The section passed in front of right superior colliculus and through the middle of the left superior colliculus dorsally to emerge

3 mm. in front of the pons on the right and 1 mm. in front of it on the left. There was no sign of hæmorrhage into the stump of the brain-stem but a clot about the size of three peas was lying over the stump above the tentorium. No detailed examination was made.

Animal XXVI.—Female. Post-mortem, see p 249. Decerebrated by earlier technique. Good rigidity, head to left, good reflexes, lifts head to left to noises on first day. No nystagmus.

On second day head lifted to left in reaction to sounds and this accompanied by nystagmus to left.

On third day respiration very fast. Reflexes very sluggish and almost absent. Some convulsive movements of the legs, but no eye movements. Died during the night.

The nystagmus when seen was of a usual type with rapid and slow components, but the animal described above and animal IX which developed nystagmus on the ninth day when meningitis occurred were the only ones where it has been observed, except in the first few hours after operation.

(j) *Glycosuria.*

It has been suggested by J. Mellanby [41] that there is a centre in the brain above the medulla which controls sugar metabolism, this theory having been built up on the prolonged glycosuria which follows decerebration as compared with that seen after decapitation. But Mellanby's decerebrate preparations were made by Langley's [29] starch injection method, so that nothing definite was known of the real level of the lesion, nor of the changes resulting in the pituitary. At the same time the glycosuria observed was only investigated over a matter of a few hours after operation. We can, however, amply confirm the long duration of glycosuria found by Mellanby after decerebration; thus in one animal urine obtained by catheterization from the bladder twenty-four hours after decerebration still contained quantities of sugar.

On the other hand, the glycosuria does not continue indefinitely. Thus the urine of cat VIII contained no sugar on the third day; in another animal (XV) urine voided forty-seven hours after operation contained no sugar. This animal had previously voided fæces and urine about thirty hours after operation; so it appeared to have ceased to secrete sugar, at any rate after thirty hours. In no case has any glycosuria been observed after the second day—though observations on this question have only been possible in preparations kept in the incubator. Nor does it appear possible that the glycosuria ceases as

the result of loss of glycogen. In cat V urine collected on the sixth day showed no sign of sugar, and yet when the animal was killed shortly afterwards the liver gave a normal glycogen reaction with iodine. In cat XXI, urine taken from the bladder after death contained no sugar, but the liver was not normal.

The theory put forward by Mellanby does not, therefore, explain the facts—though the more prolonged glycosuria compared with that of the decapitate preparation certainly requires some explanation. Further, experiments on this point are planned for the near future. The glycosuria we have observed occurs even when the body temperature has been subnormal for quite a short while, and we do not think that it is to be explained as merely secondary to a fall in body temperature as is suggested by the experiments of Morita [44] on rabbits, nor do we find, as he did, that it ends usually only on exhaustion of the liver glycogen.

CHAPTER IV.—UNILATERAL DECEREBRATION.

A series of semi-decerebrations as chronic experiments was undertaken on the suggestion of Professor Sherrington, in order to study the resultant decerebrate rigidity. Seventeen cats were operated upon of which four died at once from hæmorrhage or accidents of anæsthesia. The remaining thirteen experiments are not sufficient to answer many of the questions that prompted the undertaking, and further work has been planned along the same line. It seems worth while, however, to include here a brief description of the semi-decerebrate preparations for the sake of comparison with the results of complete decerebration.

Operative Technique.

Cats were used under chloroform or chloroform and ether anæsthesia by the open method. A small mid-line incision was made in the neck and the right carotid tied. The left carotid and vertebrals were controlled at the proper time as in the bilateral operation. The skin and muscle were reflected from the right side of the head. The underlying skull was quickly removed so as to expose the right cerebral hemisphere. The dura was reflected. Then, with the arterial supply shut off, the operator passed a flat bone spatula (a properly shaped salt-spoon) over the top of the right cerebral hemisphere, until it touched the falx, and swept it downwards to the tentorium and outwards, carrying

away all of the hemisphere except the frontal pole, which could be quickly scraped out. A part of the inferior colliculus was usually thus left intact. This was reflected forward from the surface of the cerebellum and removed by a bent bistoury, together with any of the mid-brain that may have remained ventrally above the top of the pons. The cavity was quickly filled with cotton wool in hot saline and the vertebral arteries released. Bits of fresh muscle were usually necessary to arrest all bleeding before the left carotid artery was released. The cavity was filled with physiological saline before closure.

In six of the experiments the cavity was filled with a melted paraffin-vaseline mixture after removal of the hemisphere. One of these animals lived only eleven hours, and four died on the day following operation. Three of the animals became dull and vomited just before death. Compression beneath the wax was suspected, and when the sixth animal became dull two days after operation the wound was opened and the paraffin removed. There was a gush of fluid from beneath showing increased pressure. The animal improved temporarily, but died on the day following from broncho-pneumonia. Examination of the brains where the dead space was filled with saline, as described above, showed a varying amount of swelling of the remaining hemisphere across the mid-line. The animals whose cranial cavities were filled with normal saline rather than wax lived to between two and forty-two days after operation. The conclusion is evident: that swelling of the remaining brain tissue against the wax was sufficient to cause fatal compression of the lower centres.

It was found advisable to suspend the more active animals in a hammock provided with slits for the legs to come through.

The removal, which was always on the right side, extended in each case down to the mid-brain. Two types of removal were made: (1) anterior, where the decerebration passed above the inferior colliculus, leaving a varying amount of superior colliculus intact and most of the mid-brain ventrally (in this type the red nucleus was not molested); (2) a posterior removal where the section passed from behind the inferior colliculus dorsally, to the anterior margin of the pons ventrally. In this type one red nucleus was removed. Post-mortem examination showed that the removal followed the median sagittal plane with surprising accuracy, except for the fact that in two cases the spatula passed about 2 mm. to the right of this plane, leaving that thickness of mid-brain and thalamus, and in several cases a very small amount of the left thalamus or mid-brain was removed.

Forced Movements and Attitude of Head.

The animal's head was *usually* held to the left at the close of the operation, and in *every case* eventually. This attitude depended on rotation of the occiput downward and to the left, so that the chin was up on the opposite side and the neck bent to the left. The displacement therefore consisted of retraction of the neck and clockwise rotation of the head on the shoulders, the head being carried to the left away from the side of removal. Those that were able to walk fell to the left or walked around in a circle to the left. If the animal was laid on its right side it raised its head up to the left and, pushing with the right fore limb, rolled about the cage. When lying on the left side the preparation frequently lay quietly but pressed the occiput against the floor. These attitudes were eventually assumed in every case (except that in two animals no note was made of any forced circus movements). In all of the anterior sections, as described above, and in the one posterior section where about 2 mm. thickness of the mesial portion of the mid-brain and thalamus were left intact, the animals turned their heads first to the right on recovering from the anæsthetic. Within one to five hours in each case this movement was reversed and the typical movement of the head to the left appeared, associated with forced movements to that side. The short duration of this preliminary turning to the right in the anterior section cases before reversal suggests that some structure is spared by the anterior or lateral removal, which is stimulated by traumatic irritation, but later becomes paralysed or unable to cope with a contrary tonic influence.

After the effects of stimulation had passed off, the head was held constantly in a position similar to what has been termed the cerebellar attitude. In lesions of one side of the cerebellum, the occiput is said to turn in that direction and the head to be retracted to the side of the lesion. In semi-sections of the mid-brain, at either a high or a low level, the movement is *away* from the lesion. This was a constant finding in these experiments. It may be explained perhaps by the fact that one side of the cerebellum is in close anatomical relation with the other side of the mid-brain. Muskens [45] has made extended observations on the effect of lesions confined to the posterior longitudinal bundle. Circus and rolling movements followed such injuries. It is difficult to make explicit applications of his results to the movements described here however.

The Side of Permanent Extensor Rigidity.

Sherrington noted in 1898 [54], working with acute experiments, that unilateral decerebration through the mid-brain was followed less regularly by decerebrate rigidity than complete sections of the brain-stem. It appeared most often on the same side as the decerebration and was occasionally observed to subside and reappear. He noted in a monkey and in cats that after right semi-decerebration, the right limbs were held in tonic extension, the tail incurvated to the right with the concavity to the right. The head was turned to the right and retracted. The left fore limb and knee were distinctly more flexed than would be expected in paralysed limbs. Thiele [57], in acute experiments, likewise noted ipsilateral rigidity after semi-section of the mid-brain, and that if the section were more anterior, through the superior colliculi, the rigidity tended to become *contra*-lateral, only a little remaining on the ipsilateral side.

The chronic experiments described below show that some of the above post-operative reactions are reversed after an initial stage of stimulation.

In the following experiment, No. P1, after removal of the right hemisphere down to the mid-brain, the preparation was suspended in a hammock in erect position with legs passing through hammock holes. The animal's head was at once turned to the right and there was extensor rigidity in all four limbs. There was slow nystagmus with the quick component to the right. At intervals there were spasms of running movements during which periods the nystagmus became more rapid. The rigidity of the left limbs became progressively less marked until two and a half hours after the close of the operation, when the right fore and hind limbs were found to be still in tonic extension sufficient to support the weight of the body. Both left limbs, however, tended to assume a flexed posture and were held thus a little rigidly. The spontaneous nystagmus had disappeared. At intervals spasms came on resembling those mentioned above, except that now the right limbs ran and the left limbs became still more flexed, especially the fore limb. At these times the eyes opened, the head turned to the right, and there reappeared a very small amount of nystagmus to the right. Left pupil widely dilated, right pupil less so. Rectal temperature 37° C.

Four and a half hours after operation—head was now turned constantly to left.

Twenty-four hours after operation—head to left and body, including tail, curved with the concavity to the left. Extensor rigidity marked on right side. Left limbs held in tonic flexion so as to resist passive extension. Occasional clawing spasms, at which times the head was retracted. The preparation was

taken from the hammock and it swallowed some milk which was poured into its mouth.

Three days after operation there had occurred a surprising change. The extensor rigidity was now in the left limbs. When suspended in the hammock and quiet, the right limbs maintained a flexed position. It was not possible to say whether there was any flexor tonus however, as the right limbs were now voluntarily snatched away when touched and were used to scratch the observer's hand whenever he attempted to administer food. The left limbs were never used in this way. When placed on the floor the animal walked slowly in a circle to the left, reeling and falling to the left. The head was still held to the left and the jaw tightly clenched. The pupils were now equal. Temperature 38° C. Late the same night condition unchanged.

Four days after operation. The front end of hammock had fallen, so that the animal's head hung almost straight down. Animal dead.

Post-mortem: A subdural hæmorrhage was found extending over the left hemisphere, under the base of the brain and down the cord to the upper dorsal region. Some of the hæmorrhage appeared to be more recent than other parts. The operative removal extended back to the middle of the inferior colliculus but had not quite come to the mid-line, so that 2 mm. of the mesial part of the mid-brain and 3 to 4 mm. thickness of the posterior part of the right thalamus were spared. A very thin slice of the mesial part of the frontal lobe was likewise spared. Interrupted serial sections were cut of the whole left hemisphere, mid-brain, pons, and medulla. There was no area of destruction or softening.

It seems probable that the behaviour of the cat immediately following the operation was due to stimulation which gradually subsided during the succeeding two days. During that time various reactions disappeared or were replaced by opposite reactions. The early rhythmic intensification of these reactions also suggests a response to irritation, i.e., clawing or running spasms associated with nystagmus to the right, head turning to the right and increase in the left-sided flexor rigidity. The spontaneous nystagmus disappeared a few hours after operation. The head, which had been first thrust to the right, came later to the mid-position and shortly afterwards was turned to the opposite side, to remain constantly in this typical position with corresponding curving of the body to the left. The occasional spasms of running movements continued for two days. At the end of that time the flexor rigidity of the left limbs disappeared and was replaced by extensor rigidity; while the extensor rigidity disappeared on the right side to be replaced by the position of flexion in the right limbs when at rest.

The unusually long duration of the signs of stimulation may possibly be explained by the evidence of older hæmorrhage at autopsy, which

had not been enough to cause compression until the accident which led to the animal's death.

Shortly after operation this animal resembled those described by Sherrington in acute experiments. Extensor rigidity was present on the same side as the decerebration, but *after* the irritation stage had passed off it was on the contralateral side. The same was true of all other animals where the section passed through the anterior part of the mid-brain. Extensor rigidity appeared on the contralateral side either at once or after a preliminary stage of flexor rigidity.

Variations after Posterior Semidecerebration.

On the other hand, when the level of removal was through the lower mesencephalon or junction of the mesencephalon and pons, the results were less constant and subject to less symmetrical variations. For example, take the following experiments:—

P2. The removal was of the posterior type. Bilateral-extensor rigidity developed on the first day. On the second day a varying degree of flexor rigidity of the left fore-limb appeared, with extensor rigidity of the other three limbs.

Experiment P3 showed, one hour after operation, extensor rigidity of the left fore-limb, the other limbs being flaccid. At the end of five hours the left fore-limb showed flexor rigidity, the other three extensor rigidity.

Experiment P4. Bilateral-extensor rigidity with considerable retraction of head associated with the usual turning to the left.

Experiment P5. A more detailed account of this animal is given on page 234, but it may be noted here that on the day of the operation there was bilateral rigidity. This was followed by some variation and then for several days, when not moving about, the fore-limbs were held in rigid flexion, the head held to the left and the neck flexed sharply on the fore-paws, while both hind-limbs went into tonic extension. This was followed by weeks of activity associated with a variable amount of extensor tone in the left fore and hind limbs.

This variation in the tone of the flexor and extensor systems in posterior removals suggests that some structure responsible for preserving a symmetrical tone pattern has been injured.

Flexor Rigidity.

After more anterior semi-decerebrations, the post-operative pattern was tonic-extension in the limbs on one side and tonic-flexion in those of the other. In certain cases, e.g., P1, the extensor rigidity appeared

first on the ipsilateral side with flexor rigidity on the other side. This was, however, shortly reversed.

It may be suggested in unilateral removal, after all stimulation effect has passed off, that control has been removed from some structure whose unantagonized action produces tonic-extensor rigidity in the contralateral limbs and tonic-*flexor* rigidity on the ipsilateral side. When the decerebration is bilateral the flexor element usually disappears and is superseded by extensor rigidity on both sides. But, as is shown elsewhere in this paper (Exps. III and IV, p. 199), even in the complete decerebration experiments, tonic-flexion occasionally replaces tonic extension.

Thiele [57] and Graham Brown [9] found that electrical stimulation of one side of the mesencephalon in the region of the red nucleus produced ipsilateral flexion and contralateral extension. The latter observed that there was an after-discharge following cessation of stimulation. It is difficult to be certain exactly what tract is stimulated by these workers. Bilateral stimulation produces bilateral extension. Their work indicates that there are structures in the mid-brain, possibly the red nuclei, which take part in the control of posture. (Also Magnus [40].) It is not necessary, nor possible, to identify this postural mechanism with that responsible for flexor or extensor rigidity.

One of the conclusions that may be drawn from these chronic preparations is that there is a mechanism by means of which there may be induced increase of tone in flexor muscles at the expense of tone in the muscles of the extensor surfaces. This flexor rigidity tends to alternate with extensor rigidity, appearing frequently in the limbs of the side opposite to that in which extensor rigidity occurs.

Wilson [63] describes decerebrate attitudes in clinical cases associated with mesencephalic lesions. In his fig. 13, p. 247, the child has assumed a position resembling the attitude of unilateral decerebrate rigidity, with arm and leg of one side extended, as the author points out. It is interesting to note, however, that in addition the limbs of the opposite side are held in a sharply flexed attitude.

Eye Changes.

In every case where the corneal reflex was examined it was present on both sides. There was some variation, but the right pupil was dilated in the great majority of cases. This was most noticeable on the

first day after operation. Nystagmus was observed only in one experiment. This was in P1, see p. 230, and passed off with other evidences of stimulation. The quick phase was toward the side to which the head was turned.

Temperature Control.

Most of the animals preserved some power of temperature control if not exposed to extremes. In three experiments there was no evidence of control whatever, the temperature falling to between $34^{\circ}5$ C. and $24^{\circ}5$ C. Those animals which survived longest maintained a normal temperature. In experiment P5 it was noted in a cold room that the animal shivered equally in the limbs of the two sides. In this animal the removal extended down to the anterior end of the pons and was carried well over to the mid-line. Removing the other half of the brain at the same level would have put an end to shivering (see p. 205).

Experiment P5 was described in part above, but as the animal lived forty-five days before being sacrificed, a brief account of the post-operative behaviour may be added.

The right side of the brain was removed up to the mid-line and down to a level below the inferior colliculus. The cavity was filled with saline. After the operation the right pupil was found to be dilated, the left contracted, both corneal reflexes present. For two days there was bilateral extensor rigidity which became variable. The animal was examined by Dr. Henry Head and Dr. Riddoch, who called attention to the fact that when it lay on the left side the left fore-limb was held in tonic flexion with claws extruded, and that ten minutes after turning over on to the right side the right fore-limb assumed the flexed attitude. This was not a constant finding at later examinations. The head was consistently turned to the left and the body and tail curved with concavity to the left. Milk was swallowed when placed on the back of the tongue with a tube. The animal clawed with right paws only. On the third day the fore-limbs were flexed sharply and paws crossed with the head bent down upon them and with occiput a little to the left. Both hind limbs were extended strongly most of the time. When disturbed there resulted spitting and clawing or purring appropriately. This continued for four or five days with gradually increasing activity. During the first week the temperature fluctuated between 40° C. and $37^{\circ}8$ C. After this the temperature settled down to normal, about $38^{\circ}6$ C.

Between one month and six weeks after operation the following notes were made. The cat had gained in weight. The head was rotated still, with occiput to the left and chin to the right, the neck, body and tail being curved with the



FIG. 6.—Experiment P5. Six weeks after complete removal of right side of brain, including mesencephalon. Tail curved to left, left legs extended, toes of left hind paws fanned, both fore paws rotated with pads a little towards the right. All of these attitudes are characteristic, as well as the rotation of the head on the shoulders.



FIG. 7.—Same animal as fig. 6.

concavity to the left (see figs. 6 and 7). When not lying quietly, the animal walked around in a circle to the left. She purred frequently and growled or spat occasionally. Even when restless from hunger, she never discovered meat or milk placed before her unless her nose was pushed down into it, resembling Goltz's dog in this respect. After she realized what it was, she ate or drank almost normally until satisfied.

Cranial nerves: She gave no evidence of smelling food from any distance but may have done so at close range. She was blind, bumping into objects frequently or walking off the edge of a board unawares. Her eye grounds were examined by Mr. Leslie Paton, who made the following note: Right optic disc chocolate colour with a sharply defined ring of very glistening green around it. Vessels normal in calibre. Upper part of fundus shows a little speckling of green passing down to a deeper green in the lower part. Left optic disc much the same as the right. The eye movements were examined by Dr. Gordon Holmes. The external ocular movements were normal and the range to either side seemed to be full. The right pupil did not react either directly or consensually to light, while the left pupil contracted to light in either eye. The right pupil did contract with some movements of the eyes, however. Also, tickling the nose or blowing into the eye caused very definite contraction of the right pupil. Reaction to pin prick and corneal reflex indicated intact fifth nerve on both sides. Hearing was acute and sounds were well localized. All other cranial nerves appeared normal.

Extremities: There was considerable variation but on the whole there tended to be tonic extension of the limbs of the left side (the opposite side to the removal). When suspended, the left limbs were extended and the hind toes fanned (see fig. 6). The left fore-paw was inverted and the right fore-paw everted. The knee jerks varied but the left was usually the more brisk.

Sensation: Pinprick was resented equally on the two sides. Touching the hair on the right side produced a reaction. The same stimulus on the left flank was ignored.

Heat control: Shivered symmetrically when in a cold room.

Gait: The right fore-foot took a longer step than the left and the foot was raised higher. She turned in a large circle to the left. Occasionally she stepped on the dorsum instead of the plantar aspect of the left fore or hind paw, and the left hind-paw at times interfered with the fore-paw. When excited, she walked about in a very small circle. It was noted by Dr. S. A. K. Wilson that the left fore-foot was advanced at each step with a tremor of the paw. At times she stumbled to the left.

Affective reactions: She purred when stroked or after feeding, growled when eating meat, and occasionally spat and scratched. When another cat was brought near her, no notice was taken until the visitor mewed. Then P5 growled and became suddenly rigid as though listening. After a little time she started toward the visitor who was moving softly, and continued until her nose bumped into the visitor. Then P5 leaped back and stood with all hair raised back and tail. The visitor moved away and at that moment P5 struck out

as though to attack her, spitting. The visiting cat was removed and P5 walked around very rapidly in a small circle.

Six weeks after the operation, the animal in excellent physical condition was sacrificed under ether-anæsthesia. Post-mortem examination showed the right side of the brain to have been thoroughly removed up to the mid-line. Several shreds of what may have been cortical tissue were left. These were not connected with the brain-stem. The right thalamus and mid-brain were removed down to a plane which passed through the anterior margin of the pons ventrally, and just behind the inferior colliculus dorsally. A complete microscopical report could be made as an unfortunate accident destroyed most of the material while it was being prepared.

CHAPTER V.—MICROSCOPICAL ANATOMY OF SPECIMENS.

(a) *Development of the Mid-Brain.*

In lower vertebrates (e.g., fishes) the mid-brain is a centre of great importance, controlling the individual response to environment. With the development of the optic thalamus and the geniculate bodies (reptiles) the importance of the mid-brain for co-ordinating visual stimuli is decreased, and in man with the elaboration of the visual cortex the anterior corpora quadrigemina of the mid-brain become rudiments. There is likewise a forward displacement of the sensory centres to the ventral part of the thalamus, which continues to develop along with the sensory cortex. The auditory paths move out from the mid-brain to the internal geniculate body and auditory cortex. The mid-brain has therefore a progressively decreasing functional importance proportionally during phylogenetic development.

Microscopically the red nucleus of a lower vertebrate is composed of large cells of motor type from which arise the rubrospinal tracts. Higher in the phylogenetic scale there appear smaller cells in the red nucleus and, as von Monakow [43] has pointed out, it is possible to distinguish an orally placed group of smaller cells, the nucleus parvocellularis of Hatschek [19] or chief nucleus, from the more caudal giant cells, or nucleus magnocellularis. The small-celled nucleus develops *pari passu* with the thalamus and cerebral cortex and is connected with them. In anthropoids and man this nucleus of small cells makes up the major part of the red nucleus, while the giant-celled part has become very small and, as a result, the rubrospinal tract has greatly diminished in volume. Nevertheless, because of the great increase in size of the small cell part, the red nucleus of man is almost twice as

large as that of the cat in proportion to the vertical diameter of the mid-brain of each species [43].

(b) *Anatomy of the Mid-Brain.*

The anatomy of the mid-brain of a cat may be quickly reviewed by reference to fig. 8, which is a drawing from a lateral longitudinal section through a cat's brain. It will be seen that a section through the mid-brain may leave or remove according to its level a number of

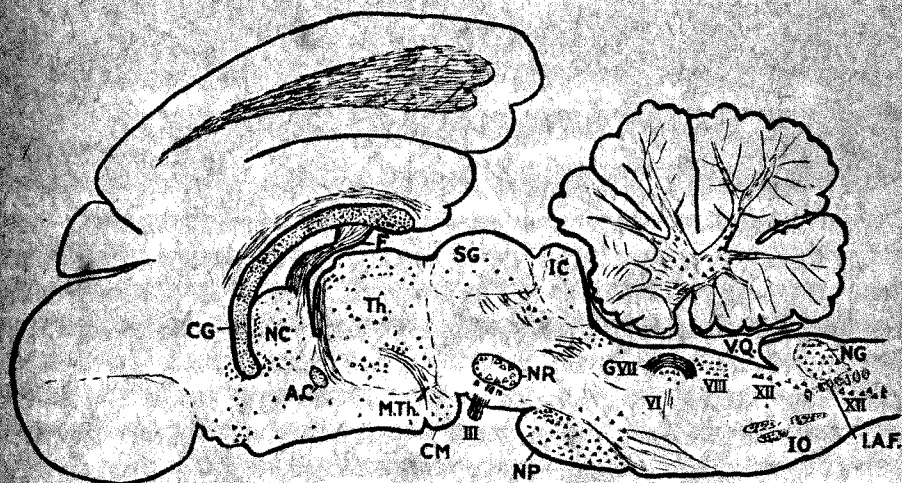


FIG. 8.—Sagittal section of cat's brain a few millimetres from the median plane, drawn from two adjacent sections, one stained by Loyez's hæmatoxylin method and the other by Nissl's method. This as well as all the other microscopical drawings was made with the help of an Edinger Drawing Apparatus kindly loaned by Dr. Gordon Holmes. Diagrams in succeeding figures are taken from this drawing reduced to natural size. C.C., corpus callosum; N.C., nucleus caudatus; A.C., anterior commissure; F., fornix; Th., thalamus; M.Th., mamillo-thalamic tract or bundle of Vieq d'Azyr; S.C., superior colliculus; I.C., inferior colliculus; N.R., nucleus ruber; N.P., nuclei pontis; III, root of III nerve; G.VII, genu of VII nerve; VI, nucleus and root of VI nerve; VIII, dorsal nucleus of VIII nerve; XII, nucleus of XII nerve; V.Q., fourth ventricle; I.A.F., internal arcuate fibres splitting XII nucleus.

structures, the anterior and posterior corpora quadrigemina, the third and fourth cranial nerve nuclei, the whole of the tegmentum, the red nucleus, &c. The red nucleus is circumscribed by a felt-work of fibres. The caudal two-thirds of the nucleus is made up of giant cells as indicated. The oral one-third only is made up of small cells.

According to Hatschek, this phylogenetically younger nucleus parvocellularis is in relation with the nucleus dentatus of the cerebellum, while the older nucleus magnocellularis is interposed between the

cerebellar nucleus globosus and emboliformis above and the descending rubrospinal tract. He concludes that this close anatomical relationship of the nucleus magnocellularis with the cerebellum and Monakow's bundle constitutes the primitive path of nerve impulses for automatic movements. Other tracts converge on the red nucleus. Von Monakow describes a fronto-rubro-tegmental pathway. The fibres thus indicated arise in the frontal cortex and pass down via the red nucleus to the tegmentum of the mid-brain and formatio reticularis of the pons, from where they are supposed to send a relay to the spinal cord. Wilson [62] has shown that there is a considerable tract of fibres from the globus pallidus which passes across Forel's field to the anterior capsule of the red nucleus. The principal red nucleus efferents are the rubrospinal tracts of Monakow which cross the mid-line in the fountain decussation of Forel. This tract arises wholly in the giant cells, according to Cajal [10]. Von Monakow describes some fibres as coming from the cells of medium size. Certainly the tract arises chiefly from the nucleus magnocellularis, and comparative anatomical studies show that this part of the red nucleus varies directly in size with that of the tract in most animals, and both are small in man. Efferent fibres of importance also pass from the red nucleus to the tegmentum and formatio reticularis, as well as to the thalamus and frontal cortex.

Because of its venerable phylogenetic history and its wide anatomical connections, the red nucleus has been rather heavily burdened with theoretical functions. It is therefore of importance to note carefully the state of preservation of this nucleus in the experimental animals.

(c) *Results of Anatomical Examination.*¹

Animal I.—Death on the eighteenth day after decerebration. Post-mortem performed about thirty minutes after death, immediately after removal from bath. Along the scalp incision there was an area of superficial cellulitis. No evidence of intracranial tension. A lump of wax filled the cranial cavity conforming to its outline. On removing the wax a thin layer of pus was found beneath it. The brain-stem and spinal cord were removed and placed in formol. See photographs of brain-stem, figs. 9 and 10. Incision A—B, fig. 9, corresponds to line A—C, fig. 11.

¹ In a number of experiments the preparations died and remained in the warm bath long enough for the brain-stem to become soft. In such cases no microscopic examination was possible.

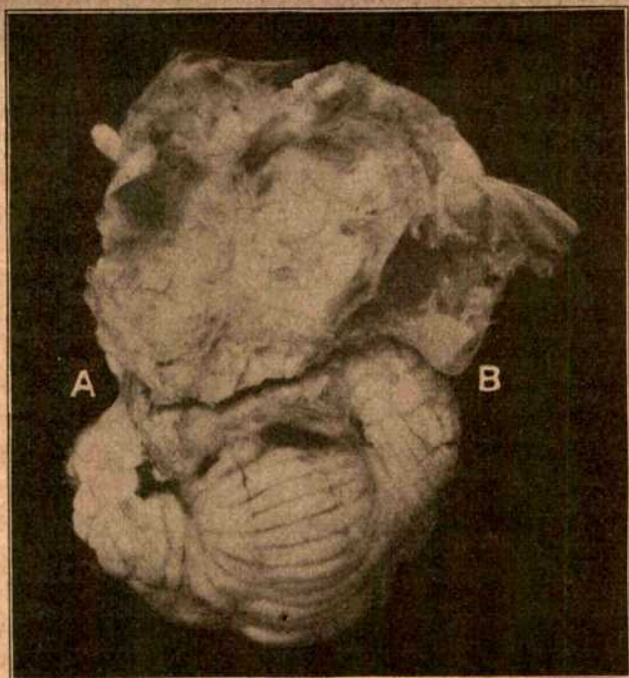


FIG. 9.—Experiment I. Photograph of brain-stem taken from above the cerebellum.

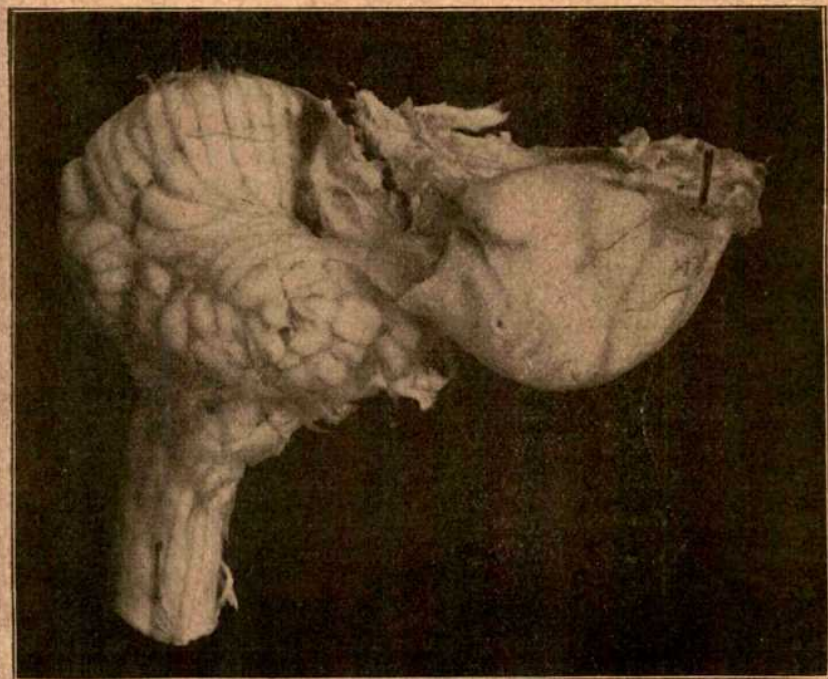


FIG. 10.—Experiment I. Lateral view of brain-stem showing the temporal pole which was not removed.

The only remaining portion of the cerebral cortex was a small part of the right temporal lobe which was attached to the brain-stem by a thin piece of nervous tissue overlying the infundibulum. Thus the pituitary and probably its blood-supply were preserved. All of the basal ganglia were removed above line A—B, fig. 11. A little below the



FIG. 11.—Experiment I. All of the tissue above line A—B was removed. A second incision at line A—C was almost complete as indicated. Dotted area represents extent of softening on right side.

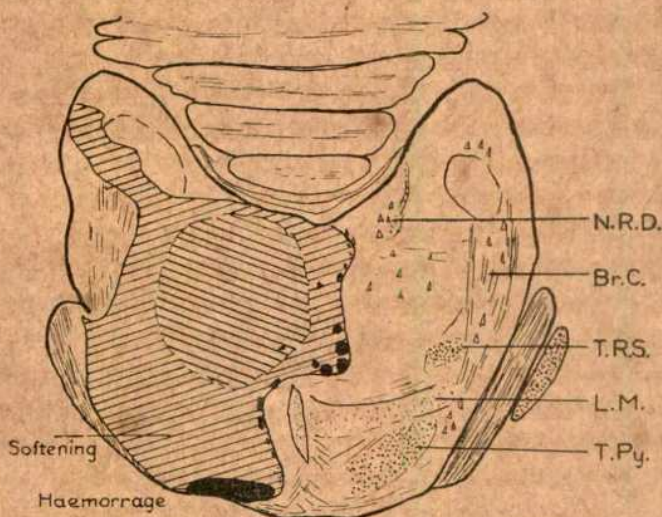


FIG. 12.—Experiment I. Drawing made with the aid of an Edinger apparatus, from a section stained by Loyez's haematoxylin method for the fibre tracts. The cell groups indicated by small triangles were added from the next section in the series stained by Nissl's method. The large area of softening has an outer part filled with compound granular corpuscles and an inner area which contained no cellular elements. N.R.D., nucleus of descending or mesencephalic root of V nerve; Br.C., brachium conjunctivum; T.R.S., rubro-spinal tract; L.M., medial lemniscus; T.Py., pyramidal tract.

level of the tentorium was an incision A—C, almost entirely severing the brain-stem. It began dorsally just behind the inferior colliculus and passed ventrally on a plane just caudal to the anterior end of the pons, but did not quite completely sever the cerebral peduncles. This incision had severed the right fifth nerve close to the pons.

After fixation, block I, including the tissue above and below incision A—C, and block II, just below this, were cut in series and alternate sections were mounted and stained by Nissl's method and by Loyez's hæmatoxylin method. The latter method demonstrates the tracts clearly. The rest of the central nervous system was stained by the Marchi method for degenerated fibres, and cut and mounted in series.

Microscopical examination shows that the red nuclei are present in the segment of nervous tissue above the incision A—C. All of the giant cells in both nuclei show marked chromatolysis, although the medium and small sized cells were for the most part normal. This indicates that the descending fibres of Monakow's bundle had been severed. Immediately below the incision A—C was an area of softening occupying practically the whole of the right half of the upper pons, as shown by the heavily dotted area in fig. 11, and passing across the mid-line dorsally. This area (see fig. 12) was separated by a line of hæmorrhage from the normal tissue of the left side. Even had the descending red nucleus fibres of this side not been severed by the incision A—C, they would have been destroyed in this area of softening. There was no evidence of encephalitis anywhere within the nervous tissue. The softening was evidently the result of hæmorrhage at the time of operation. If the experiment had been acute instead of chronic, it is quite possible that this area would have been passed as normal, although it was doubtless functionally inactive from the start.

The cerebellum was normal and it should be noted that although there was, of course, interruption of the tract connecting cerebellum with red nucleus and thalamus, the ventral spino-cerebellar tract of Gowers was intact and showed no degeneration. There were degenerated fibres in the middle cerebellar peduncles, as would be expected from the injury to the nuclei pontis, and there were a few degeneration granules in the restiform body. Vestibular nuclei were intact.

The Marchi sections beginning in the pons and passing downwards showed degeneration as follows. (Refer to drawings, figs. 13, 14, 15, 16, 17, 18; black dots indicate degenerated tracts.)

(1) The pyramidal tracts show rather fine degeneration-granules. It was noted that immediately below the pons degenerated fibres came off from the pyramidal tracts, decussated at once and passed outward among the fibres of the trapezoid body (fig. 14). They could not be definitely traced beyond the superior olivary nucleus and the medial trapezoid nucleus. Below the corpus trapezoidium also, the decussation of these pyramidal fibres continued. Their ultimate destination

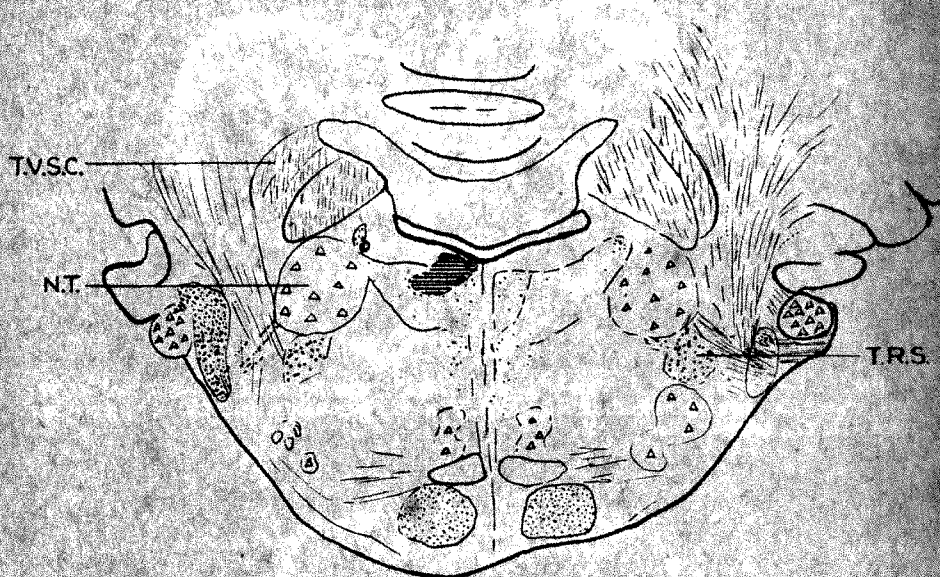


FIG. 13.—Experiment I. Section prepared by Marchi's method to show degenerated fibres. The area of softening described above (fig. 12) is represented at this level only by a small area beneath the fourth ventricle. T.R.S., rubro-spinal tract; N.T., nucleus of trigeminal nerve; T.V.S.C., ventral spino-cerebellar tract.

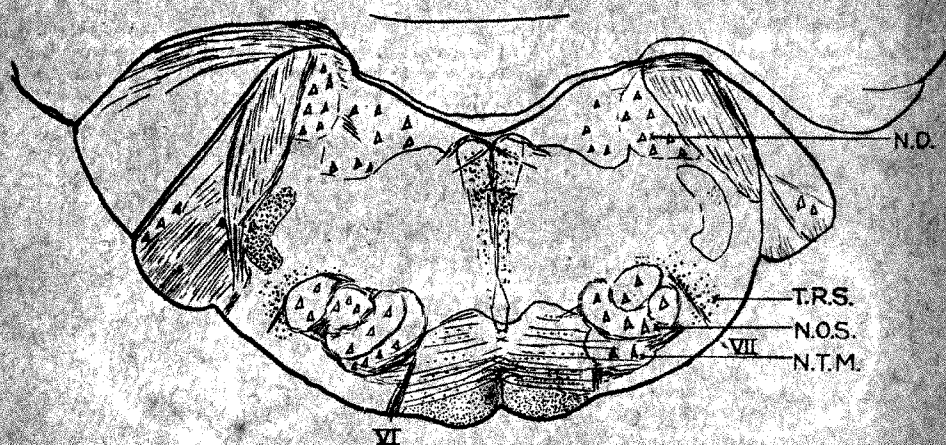


FIG. 14.—Experiment I. Marchi stain. Degenerated fibres may be seen to decussate in the mid-line and pass outward in the trapezoid body as far as the medial nucleus. N.D., Deiters' nucleus; T.R.S., rubro-spinal tract; N.O.S., nucleus of the superior olive; N.T.M., medial nucleus of the trapezoid body.

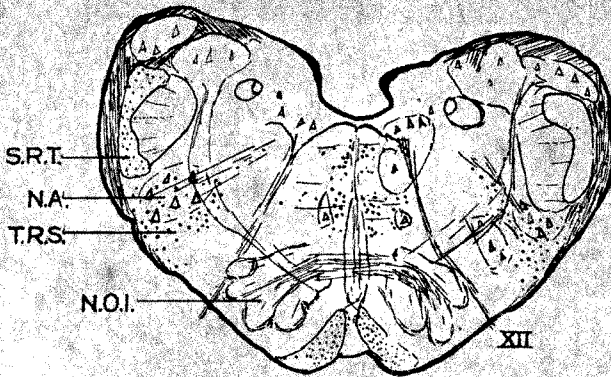


FIG. 15.—Experiment I. Marchi stain. S.R.T., sensory root of trigeminal nerve; degenerated fibres due to section of the nerve; N.A., nucleus ambiguus; T.R.S., rubro-spinal tract; N.O.I., inferior olive.

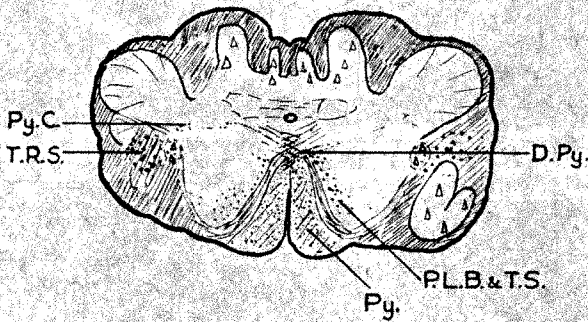


FIG. 16.—Experiment I. Marchi preparation. The degeneration granules of the decussating pyramidal fibres are finer than those of the rubro-spinal tract. It is no longer possible to distinguish tecto-spinal tract from posterior longitudinal bundle. Py., pyramidal tract; Py.C., crossed pyramidal tract; T.R.S., rubro-spinal tract; D.Py., decussation of the pyramids; P.L.B. & T.S., posterior longitudinal bundle and tecto-spinal tracts.

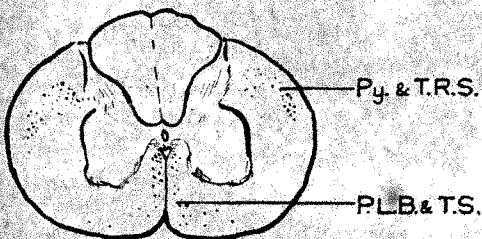


FIG. 17.—Experiment I. Spinal cord at the level of 5th cervical segment. Py. & T.R.S., pyramidal and rubro-spinal tracts; P.L.B. & T.S., posterior longitudinal bundle and tecto-spinal tracts.

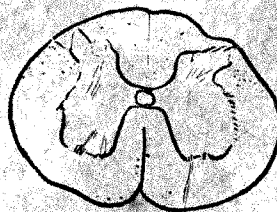


FIG. 18.—Experiment I. Section from 6th lumbar spinal segment. Degenerated fibres persist in both ventral and lateral columns.

could not be determined except that there seemed to be an increase in the number of scattered degeneration-granules in the formatio reticularis. In a personal communication Dr. Gordon Holmes has suggested that these fibres may be cortico-bulbar. Further study of this tract is projected with several other possibilities in mind.

(2) Posterior longitudinal bundle presented in the pons a sprinkling of coarse granules near the mid-line. At the top of the medulla they are displaced ventrally by the bundles of entering fibres from the vestibular system. These degenerated fibres pass downwards into the ventral columns of the spinal cord, together with the fibres of the predorsal bundle from which they cannot be distinguished.

(3) Predorsal fibres (presumably tecto-spinal) pass downward from the highest section, on either side of the raphé, only distinguishable from the degenerating fibres in the posterior longitudinal bundle by their more ventral location and their denser grouping. In the cord they are indistinguishable from the posterior longitudinal bundle fibres with which they enter the ventral columns where degeneration-granules are easily followed as far as the lower lumbar segments (figs. 17, 18).

(4) The descending motor fibres or mesencephalic root of the V-nerve were found degenerated from beneath the lateral limits of the fourth ventricle to the middle of the pons, where they turned and passed through the chief sensory nucleus of the V, just lateral to the rubrospinal tract, and joined the trunk of the V-nerve. The sensory root of the V was completely degenerated on the right, due to section of the nerve at the base of the skull, and the degenerated fibres could be followed downward in the spinal root of the V. There was also a small group of degenerated descending fibres in the spinal root of the left V-nerve.

(5) The descending fibres of the rubrospinal tract were replaced by myelin granules about equal in number on the two sides and differing from the pyramidal fibre granules by being coarser than the latter. At the level of the superior olive the rubrospinal tract has moved ventrally and laterally so as to pass in a band around the lateral boundary of the superior olivary nuclei (fig. 14). The fibres then enter the seventh nucleus, which lies immediately below, and are sprinkled out among the cells of this nucleus and its caudal continuation, the nucleus ambiguus (fig. 15). A few of the degenerated fibres pass dorsalwards with the fibres of the seventh nerve-root toward the genu of that nerve, and likewise at a lower level with the dorsally

directed motor fibres of the ninth and tenth nerves from the nucleus ambiguus (fig. 15). The degenerated tract was traced directly down to its characteristic prepyramidal position in the cord.

To summarize the anatomical findings in Experiment 1: There was a small amount of pus about the wax in the cranial cavity. There was, however, no encephalitis of the brain-stem. That the red nuclei did not function after the operation is shown as follows: (1) There was chromatolysis of the caudal end of each red nucleus—the nucleus magnocellularis. (2) The incision A—C appeared microscopically to have cut across Monakow's bundle. (3) The area of hæmorrhagic softening which destroyed the whole of the right side of the brain-stem in the upper pons likewise destroyed the rubrospinal tract on that side (fig. 12). (4) There is a heavy degeneration of the rubro-medullary and rubrospinal tracts, shown by Marchi's method, about equal on the two sides. It is possible to state with certainty, therefore, that all of the mesencephalon and higher centres were removed or without connection with the rest of the organism, except that the hypophysis and its blood supply were intact. The metencephalon, except for the area of hæmorrhagic softening in the upper pons, was intact, and its neurones capable of functioning, as demonstrated by Nissl stains.



FIG. 19.—Experiment XXI.

Animal XXI (p. 221).—Death on the twenty-second day after decerebration. Cause of death, pneumonia, and intracranial infection. The decerebration was complete. All of the cerebrum and basal ganglia were removed, the line of decerebration passing through the middle of the inferior colliculus dorsally to 1 mm. above the upper edge of the pons ventrally. (Line A—B, fig. 19). Brain-stem and segments of cord were stained by the Marchi method. There was degeneration of the corticospinal, rubrospinal, and tectospinal tracts, and the posterior longitudinal bundle. Degenerated fibres were traced into the lowest dorsal segments in the ventral and lateral columns.

Animal II (p. 195).—Death on the twenty-third day after decerebration. Cause of death, accident due to lively running movements. Lungs showed evidence of recent broncho-pneumonia in recovery stage. The level of decerebration was more anterior than in the last one described, passing between the superior and inferior colliculi dorsally. The section was slightly oblique, removing more tissue on the left than on the right. No note was made of the level ventrally, but Marchi sections of the brain-stem and cord showed heavy bilateral degeneration of the

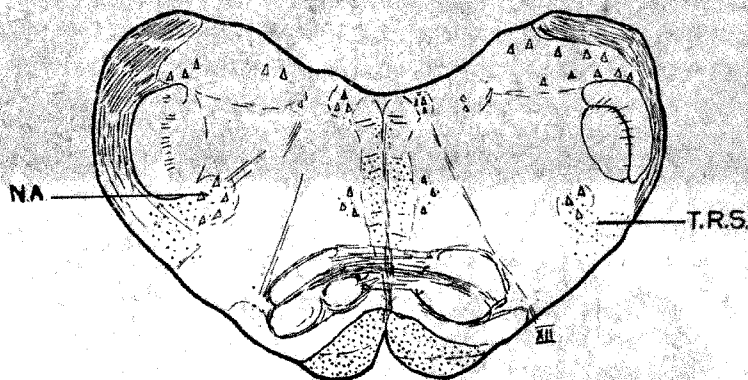


FIG. 20.—Experiment II. Marchi preparation. T.R.S., rubro-spinal tract; N.A., nucleus ambiguus.



FIG. 21. —Experiment IX.

tion of the rubrospinal tract in addition to degeneration of the other descending tracts (see fig. 20). Therefore, most, if not all, of the red nucleus must have been removed. Degenerated tracts were followed down into the lower lumbar segments in the lateral and ventral columns.

Animal IX (p. 203).—Death on the eleventh day after decerebration. Infected hæmatoma beneath wax. The level passed through the superior colliculus dorsally and just in front of the emerging fibres of the third nerve ventrally (line A—B, fig. 21). The time was not

sufficient to provide for complete degeneration, but there were a few black granules shown by the Marchi method in the pyramidal tract and posterior longitudinal bundle, and also the rubrospinal tract. One may assume, therefore, that there was some injury to the red nuclei, unless some of the fibres of Monakow's bundle have a higher origin, e.g., thalamus, as claimed by Bechterew [5].

Animal XVII (p. 218).—Death nine days after decerebration. The level was between the superior and inferior colliculi dorsally. No note was made of the ventral level but some of the hippocampus was left on the right side. Microscopic examination by the Marchi method showed degeneration in all the chief descending tracts, including the rubrospinal. The reaction of degeneration was incomplete, doubtless due to the short time which had elapsed since decerebration.

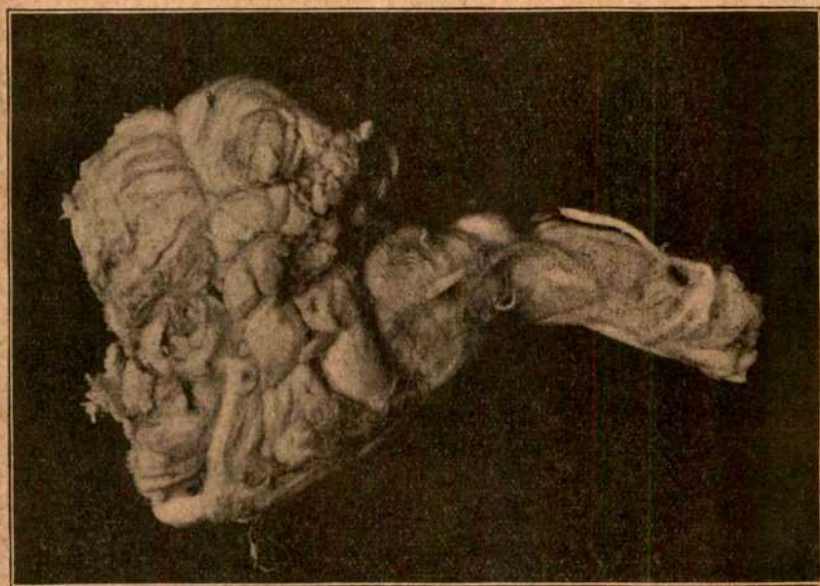


FIG. 22.—Experiment XXIII. The under-surface of the remaining mesencephalon may be seen above the upper margin of the pons.

Animal XXIII (p. 222).—Death five and a half days after decerebration. There was hæmatoma beneath the wax in the cranial cavity. The lungs were congested and there was exudate in the bronchi. The decerebration had been complete. All of the colliculi had been removed and some of the tegmentum caudal to the inferior colliculus. Ventrally, the level of incision was considerably higher, leaving 4 mm. of the left

cerebral peduncle above the pons, and 2 mm. of the right. See photograph of the brain-stem, taken from the left side (fig. 22), also schematic representation of the level (fig. 23). Microscopical sections were made of the top segments, by the Nissl and Loyez methods. There was no encephalitis. The red nuclei were present, at least in part, and may have been functioning.

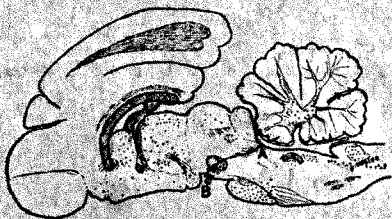


FIG. 23.—Experiment XXIII.

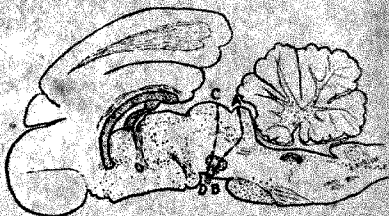


FIG. 24.—Experiment XXVI.

Animal XXVI (p. 226).—Death three days after decerebration. No cause of death could be ascertained. The decerebration was oblique, the level indicated in fig. 24 by the line A—B for the left side and the line C—D on the right side. Microscopical examination of sections through the top block of the brain-stem showed more of the red nucleus present on the right than the left. Most of the cells of the nucleus magnocellularis showed chromatolysis. The right inferior colliculus was intact. Part of the left inferior colliculus was missing.

Animal VI (p. 201).—Death two days after decerebration. No cause of death determined. The microscopical level of decerebration, which was oblique, is shown in fig. 25, by the line A—B for the left side and C—D

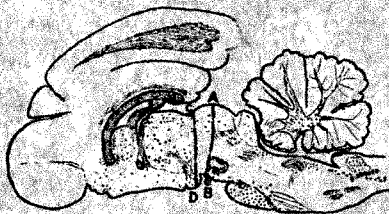


FIG. 25.—Experiment VI.

for the right side. Microscopical sections showed a circumscribed area of hæmorrhage which destroyed most of the left red nucleus and probably all. The cells of the right red nucleus were present. About half of the large cells showed chromatolysis, the rest were normal. There was no infection. Both inferior colliculi were normal and there was no interference with the lateral fillets.

Animal IV (p. 199).—Killed on the sixth day after decerebration. There was evidence of beginning broncho-pneumonia. The decerebration was complete except for a piece of the left crus, which was attached to the pons by a narrow strip of tissue. The pituitary was intact with its blood supply. The macroscopical level of decerebration is shown by line A—B, fig. 26. Microscopically the whole top of the

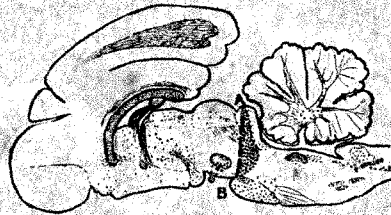


FIG. 26.—Experiment IV.

brain-stem was softened and infected, except the narrow strip of pyramidal fibres where the piece of cerebral peduncle mentioned above was attached. There was an area of hæmorrhage in the right proximal half of the pons, destroying the formatio reticularis here. There was no encephalitis in the deeper segments of the pons. The cells of the vestibular nuclei and the nuclei of Deiters were for the most part normal, but large cells in the formatio reticularis (called nucleus salivarius superioris by Winkler and Potter [64] all showed chromatolysis, suggesting that their axones had been sectioned. There was no evidence of red nucleus anywhere.

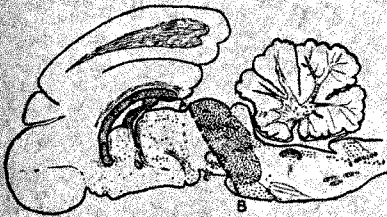


FIG. 27.—Experiment V. Left side.

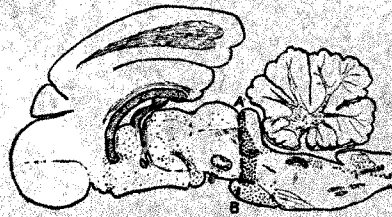


FIG. 28.—Experiment V. Right side.

Animal V (p. 200).—Killed in apparently good condition on the sixth day after decerebration. There was ophthalmia of the right eye and the right V nerve was damaged near its exit from the pons. The level of decerebration as seen microscopically passed through the superior colliculus on the left side (A—B, fig. 27), and between the two colliculi on the right side (A—B, fig. 28).

Ventrally it came below the upper margin of the pons, but there was a small block of tissue attached by some of the fibres of the crura cerebri to the pons. This overlay the pituitary whose blood supply was apparently intact. There was a considerable hæmorrhage extending down into the pons and causing destruction of almost all the normal tissue indicated in the dotted areas of figs. 27 and 28. There was cuffing of the vessels with polymorphs showing that there was some encephalitis of the superficial areas in addition to the softening due to hæmorrhage. Such of the decussation of Meynert and Forel as may have existed was completely destroyed. Careful microscopical examination showed the red nuclei removed or destroyed by hæmorrhage. On the left side the formatio reticularis was destroyed at least as far down as the middle of the pons. On the right a few nerve cells could still be recognized in parts of the upper pons, but they were not normal as shown by Nissl staining. The destruction did not reach as far as Deiters' nucleus.

In this case it is certain that the red nucleus on both sides was completely destroyed. Much of the inferior colliculi was left and microscopically normal, but all connection of these centres with the rest of the brain-stem was severed. The level of decerebration is in reality the middle of the pons.

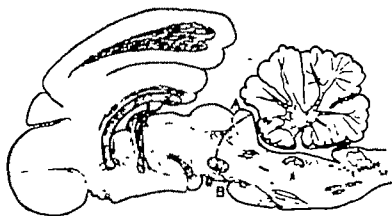


FIG. 29.—Experiment VII.

Animal VII (p. 202).—Death twenty-eight hours after decerebration. due to hyperpyrexia after warming before stove. No evidence of infection. A small amount of isolated brain tissue remained over the infundibulum. Top of brain-stem was smooth, symmetrical, and convex in outline, beginning in the middle of the inferior colliculi dorsally and the upper border of the pons ventrally. (Fig. 29, line A—B).

To microscopical examination, part of the red nucleus was present on either side and many of the cells were normal. Several small areas of hæmorrhage extended downward a few millimetres. The pons was otherwise normal.

Animal VIII (p. 203).—Death on the seventh day after decerebration due apparently to secondary hæmorrhage from the brain-stem. There was pus and blood-clot between the wax and the brain-stem. Progressive microscopical sections showed that there was no encephalitis below the superficial layers. To microscopic examination the level of decerebration passed between the superior and inferior colliculi on the right and through the middle of the inferior colliculus on the left, to end at the upper border of the pons ventrally. See figs. 30 and 31. A small amount of brain matter remained above the infundibulum. The tissue corresponding to the dotted areas was softened and filled with compound granular corpuscles.

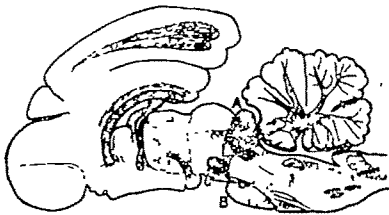


FIG. 30.—Experiment VIII. Right side.

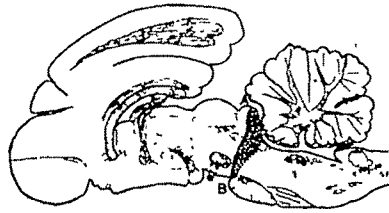


FIG. 31.—Experiment VIII. Left side

There was no remnant of red nucleus on the left side and only a few cells belonging to this nucleus remained on the other side. The interpeduncular ganglion and most of the substantia nigra cells were normal as well as the pontile nuclei. Most of the formatio reticularis was normal. With the exception of a small proportion of the cells of the right red nucleus, the level of decerebration was below the mesencephalon.

CHAPTER VI.

(a) *Decerebrate Rigidity in Chronic Experiments.*

Decerebrate rigidity was first mentioned in experimental animals by Sherrington in 1896 [53]. He described it as a "tonic rigidity in certain groups of skeletal muscles, especially those in the dorsal aspect of the neck, tail, and of the extensor surfaces of the limbs." Decerebrate rigidity in animals is, then, a tonic rigidity of the anti-gravity muscles, the muscles employed in maintaining an erect posture.

The neurogenic source of this phenomenon has been the subject of many studies. Hughlings Jackson [24] had suggested that the cause

of hemiplegic rigidity in clinical cases was due to the "unantagonized influence of the cerebellum" . . . "after the influence of the cerebrum is taken off." Similarly, the decerebrate rigidity of experimental animals has been commonly considered a release phenomenon

It has been maintained that the red nuclei were the source of the rigidity after decerebration through the mid-brain or after a lesion to the cerebellum. The intimate connection of these twin nuclei with cerebellum, thalamus, globus pallidus, and spinal cord seems to fit it for such a function. Moreover, it has been shown, notably by Graham Brown [9], that electrical stimulation of the red nuclei results in a postural response and the stimulation is followed by a well maintained after-discharge. In a different way, Magnus and his co-workers have demonstrated these postural movements also. They have described a number of position reflexes which may be seen in the decerebrate animal. Many of these position reflexes take place only if the mid-brain including the red nucleus be present. Others continue to be seen after the removal of the mid-brain. But because mid-brain and red nucleus may have to do with position mechanisms, as indicated above, it does not necessarily mean that they are indispensable for the maintenance of extensor rigidity.

The experiments reported in this paper prove that the red nuclei are *not* necessary for the maintenance of decerebrate rigidity. Inasmuch as the animals were kept for long periods of time the possibility of irritation effects disappears. The rigidity must be a release phenomenon. But it is not release of the rubrospinal tract.

Careful microscopical examination, as described above, showed for example that in experiments IV and V there was no red nucleus to be found. In experiment I, cells of the red nucleus were found in a block of tissue which was severed from the brain-stem. Below this the area through which the rubrospinal tract must have passed was completely softened and below this there was heavy degeneration of the rubrospinal tracts. In other experiments (as II, VIII, XVII, XXVI) the greater part of the red nuclei was missing and probably the remnant was not functionally active

In experiment I, just mentioned, the animal showed extensor rigidity during the early days following operation, and at times this rigidity was seen to vary in intensity during an examination. On the twelfth day after operation it was noted that the right hind-leg was rigid in flexion while the other limbs maintained extensor rigidity. In experiment IV there was extensor rigidity of moderate intensity on the first two days after operation. During the next two days a tendency was noted to assume a rigidly flexed attitude. On removal from the bath to be dried, extreme extensor rigidity appeared with retraction

of the head. This was followed by a short period of tonic flexion of the limbs and extrusion of the fore-claws. There were then several alternations of flexor and extensor rigidity.

Animal V developed extensor rigidity on the day of operation. Next day it was much increased. On the third day the extensor rigidity was marked, especially after the animal had been handled and turned in the bath. The tone was probably sufficient to support the weight of the body with ease. On the sixth day the animal was removed from the bath and dried in the incubator. During the drying process there was no rigidity, the limbs being flaccid. After this one of the nerves was dissected out for a stimulation experiment. During the dissection there were vigorous movements, micturition and the development of extreme extensor rigidity which was maintained during manipulation, but lessened when the animal was left quiet for a quarter of an hour. During further dissection extreme rigidity returned. By reference to p. 251 it will be seen that because of softening, the actual level of decerebration in this animal was the middle of the pons. Preparation VIII developed a considerable extensor rigidity in all four limbs immediately after operation. On the fourth day extreme rigidity was noted in all four limbs, but after the preparation was turned from the right to the left side the right fore-limb went into tonic flexion with extrusion of claws. Many of the position reflexes described by Magnus were later elicited in this preparation. (See p. 203.)

It is unnecessary to multiply examples. Decerebrate rigidity appears even though the red nuclei be removed. The preparations with high decerebrations acted differently, went into violent running movements, and were much more difficult to keep alive than those in which the removal was more posterior. There was perhaps more variability in the posterior removals, and the rigidity is frequently intensified by afferent stimuli. This variability was noted by Cobb, Bailey, and Holtz [11] in acute preparations, as well as the effect of afferent stimulation. Magnus [40] concluded that to remove the mid-brain resulted in the loss of the ability to bring the body to normal from any abnormal position. The difference in the behaviour of the preparation according to the level of decerebration cannot be denied. Whether or not there is any difference between the rigidity of the animals with and those without red nucleus, as suggested by Cobb, Bailey and Holtz, must be decided by myographic examination of the tonus of isolated muscles. To less refined methods of examination the rigidity when present is the same regardless of the fate of the red nuclei.

In a number of the complete decerebration experiments, retraction of the head amounting to opisthotonos appeared in preparations which at the same time showed extreme extensor rigidity and this was

frequently spasmodic. That is, head retraction appeared periodically together with an increase in extensor rigidity. It seems that when extensor rigidity becomes sufficiently intense, opisthotonos usually appears as a part of the same phenomenon, as Wilson [63] has suggested for tonic fits in man.

The term decerebrate rigidity is generally taken to mean extensor rigidity. But in completely decerebrated specimens another type of rigidity sometimes appears, tonic contraction of the muscles on the *flexor* aspect of the limbs. This is associated at times with bending of the head downward and extrusion of the fore-claws. After *semi-decerebration* this phenomenon appeared much more frequently (p. 232), alternating with extensor rigidity as though complementary to it. It would be more accurate, therefore, to speak of extensor and flexor rigidity as two types of decerebrate rigidity. Sherrington, Thiele, and Weed have independently noted the occasional appearance of flexor rigidity.

Study of the results of the more anterior unilateral decerebrations demonstrates that the extensor rigidity may be ipsilateral in the acute preparation, as described by Sherrington, but that after the stage of stimulation disappears the extensor rigidity becomes contralateral in the chronic preparation. Correspondingly, flexor rigidity, though sometimes contralateral at first, quickly becomes ipsilateral. These observations suggest that the fibres whose interruption give rise to extensor rigidity decussate somewhere between the anterior part of the mesencephalon and the upper part of medulla oblongata. This is in agreement with the experiments of Thiele.

The anatomical basis generally accepted for extensor rigidity at present is, very briefly: the rigidity is a proprioceptive reflex depending on the integrity of the local reflex arc, including the afferent and efferent paths to any muscle in question (Sherrington) [56]. The condition appears only after section of the brain as low as the posterior part of the thalamus (Thiele) [57], or the anterior part of the mid-brain (Magnus) [40]. In the chronic experiments of de Barenne there was no rigidity after removing fore-brain, leaving thalamus intact. It would seem that the tract whose interruption is responsible for decerebrate rigidity has its origin about the level of the hypothalamus.

On the other hand, section of the brain-stem below the pons immediately abolishes the rigidity on the ipsilateral side [54], but not on the contralateral side. The phenomenon is therefore independent of the pyramidal tract. The nerve paths responsible for the decere-

brate rigidity, whatever their source may be, are found in the antero-lateral columns of the cord, since cutting the posterior or the ventral columns does not influence rigidity.

There has been considerable discussion as to what is the source of the tonic influence which is brought into play by decerebration. It must be located in the pons or upper medulla oblongata. The action of this centre, or perhaps reflex arc, is modified by stimuli from the otic labyrinth although decerebrate rigidity is not abolished by section of the eighth nerve [54]. There exists an area on the anterior surface of the vermis cerebelli, stimulation of which inhibits decerebrate rigidity [53], [33], [59], [11]. Removal of this area induces this condition if not already present. Rigidity has been observed to continue for some time after total ablation of the cerebellum. Cobb, Baily and Holtz [11] maintain that the inhibitory pathway is the dentate-rubral fibres. Weed believed the cerebellum to play an important rôle in the cause of decerebrate rigidity, but the removal of the cerebellum in his experiments did not abolish it immediately. Thiele [57] reported that progressive removal of slices of the cerebellum induced decerebrate rigidity until the vicinity of Deiters' nucleus was reached, when all rigidity suddenly disappeared. This author likewise made progressive sections down the brain-stem and reported that the decerebrate rigidity which appeared when the section passed below the posterior end of the thalamus, disappeared suddenly on reaching the level of Deiters' nucleus. These were acute not chronic experiments. Magnus considers that the decerebration must be as low as the anterior part of the mid-brain before rigidity results. He describes decerebrate rigidity as a caricature of standing, inasmuch as the ability to assume and maintain an upright position disappeared with the removal of the mid-brain [40]. Magnus likewise agrees that decerebrate rigidity may persist until the level of removal reaches the lower margin of the pons.

It has been shown that the mid-brain and pons of a decerebrate preparation can be bisected in the sagittal plane without loss of decerebrate rigidity. On one occasion we confirmed this, as follows.—

A complete decerebration was performed on a cat at 11 o'clock in the morning. The level was between the colliculi dorsally and 3 mm. in front of the anterior margin of the pons ventrally. The extensor rigidity was well maintained and the preparation would stand if properly adjusted on its feet. At 4.45 p.m. a sagittal mid-line incision was made through mid-brain, pons and well down into medulla oblongata. The rigidity continued and was still in evidence at 6.15 p.m. By this time the rigidity was less intense and the

respiration was just coming to a stop. The lungs were artificially ventilated. The limbs, after a stage of clonus, improved their extensor rigidity for a time.

Examination of the brain-stem showed the longitudinal section to be complete at the level of the red nuclei. At the level of the upper medulla the bisection was complete dorsally but stopped 1 or 2 mm. short of the ventral surface, only severing a part of the inter-olivary body. In the lower medulla a considerable hæmorrhage had occurred which may have been responsible for the respiratory failure.

As the rubrospinal tract decussates almost completely in the mid-line, this is added evidence that the presence of the red nuclei is not essential to the existence of decerebrate rigidity. The experiment likewise suggests that paths which are responsible for decerebrate rigidity do not decussate in the medulla.

Nothing has been encountered in these experiments which would contradict the view of Thiele that the integrity of Deiters' nucleus is essential for the production of decerebrate rigidity, or that the spinal fibres arising in Deiters' nucleus carry efferent impulses indispensable to the reflex. Weed suggests that the ventral cerebellar tract of Gowers carries afferent impulses in the reflex circuit, which is responsible for the rigidity. This tract passes dorsally below the level of even the lower decerebrations and was seen to be intact in all of our anatomical preparations that were carefully studied.

(b) Temperature Control.

The whole literature on the subject of temperature control and the nervous mechanisms which are concerned has been so carefully reviewed recently by Barbour [1] that no attempt need be made here to give any detailed account, and reference may only be made briefly to such papers as bear most closely on the results here reported.

It has been shown by Rogers [50] that in pigeons section of the brain-stem below the level of the thalamus completely removes all temperature control, while section above the thalamus does not, so that even in birds, in which the development of the corpus striatum is very different from that of mammals, section of the brain-stem in the region we have studied destroys all temperature control. The similarity with the results obtained in cats is the more marked when the experiments of de Barenne [2] [7] are also taken into consideration. He removed practically all the brain above the thalamus in the second of the two cats described in the above paper, and yet found it to have a normal temperature control. Therefore, in cats also the control of temperature

may be definitely located between the level of the middle of the superior colliculi and 2 mm. in front of the pons below and the upper limit of the thalamus above. Such a situation for the centres controlling temperature regulation is in entire accord with the work of Barbour on the effect of localized heating of the brain.

Isenschmidt and Krehl [22] in 1912 showed that rabbits in which the brain-stem was divided at the level of the junction of the diencephalon and mesencephalon lost all power of temperature control, while if the hemispheres alone were removed control was not lost. But their animals without temperature control only survived a few days, and considering how long reactions may be depressed following a lesion, the possibility of a later return of temperature control was not excluded.

Later Isenschmidt and Schnitzler [23] made various sections in the mid-brain at different levels, these sections being often one-sided and partial, and they came to the conclusion that the heat regulation centre was in the region of the tuber cinereum. This would be consistent with our results, but their conclusions cannot be regarded as firmly established since again they were unable to keep alive for more than a few days any animals which lost their power of temperature control. Consequently they could not elaborate their results by examination for nerve degeneration. The "Zwischenhirnstich" of Leschke [31] gave similar results.

The animals that we report offer therefore strong confirmatory evidence as to the position of the centres controlling temperature, and it should be much easier to determine whether these are in the thalamus or tuber cinereum by the employment of the methods we have developed for nursing animals which have lost their power of temperature regulation.

It will be evident from the experiments that have been described that no sign of temperature control remains and that no such control returns at any rate within two weeks. The complete absence of shivering in the bilaterally operated animals and its ready occurrence after the unilateral operation is very striking, and it is of considerable interest that in the latter case shivering occurs equally on the two sides of the body. With the unilateral decerebrations it was noticed that if the remaining brain matter was exposed to some pressure (as occurred when wax was used in these cases) the raised intracranial pressure readily destroyed the power of temperature control, and it was also noticed that in the other animals which showed deficiency of temperature control the lesion had slightly damaged the left side of the brain-stem as well as the right.

It seems probable, therefore, that tracts which carry either sensory or motor fibres intimately concerned in temperature control run in the mid-brain close to the mid-line, possibly for instance in the posterior longitudinal bundle, though we have no direct evidence of this.

The animals with bilateral decerebration showed a considerable change in the respiratory rate with change in body temperature in spite of the apparent absence of temperature control. This however appears to be adequately explained by assuming that a rise in body temperature alters the respiratory rate by affecting the respiratory centre directly, just as it alters the heart rate by direct action on the heart, and that the respiratory rate may be still further quickened by the indirect action of a metabolism which has also been increased as the result of the raised body temperature. In any case the quickening of the respiratory rate with raised body temperature is probably considerably less than that occurring in the intact animal [20] [30] [48].

While up to the present these preparations have given no great additions to our knowledge of the mechanisms concerned in temperature control, the possibility of the preservation over long periods of animals, in which this control has been lost, would seem to offer many new opportunities for the investigation of this problem.

CONCLUSIONS.

(1) A technique is described which allows cats in which all the brain above the level of the pons has been completely removed to be preserved for days and occasionally as long as three weeks. The essential factor is shown to be the maintenance artificially of a normal body temperature.

(2) Chronic decerebrate preparations obtained in this way are found to maintain throughout this period the general characteristics described by Sherrington. The extensor rigidity is usually maintained with brief intermissions, and further proof is thus offered that it is a "release phenomenon." Rigidity continues in many cases after full degeneration of the divided tracts has occurred.

(3) Decerebrate rigidity is described lasting for more than two weeks in animals in which all the red nuclei can be shown histologically to be no longer functioning. Decerebrate rigidity can therefore occur in the absence of the red nucleus, and although many reactions and position-reflexes disappear in the more posterior decerebrations, the character of the extensor rigidity seems to be the same. It was

sometimes found that sensory stimuli would increase the rigidity already present, or cause it to reappear if it were absent.

(4) Decerebrate rigidity is probably dependent on some centre or reflex arc at about the level of Deiters' nucleus. None of our histological examinations showed any lesion to this nucleus nor to the ventral spino-cerebellar tract of Gowers, and the rigidity did not disappear after mid-line sagittal section of the pons and medulla.

(5) Head retraction accompanies extreme rigidity, but is only seen with other evidences of an irritative lesion such as may be produced by progressive hæmorrhage. It then forms a part of what may be called a tonic extensor fit which on the day of operation occasionally developed into a well marked opisthotonos. Spontaneous nystagmus sometimes appears also as the result of this irritation.

(6) The level of the section was generally rather oblique and usually more was removed on the left side; many animals showed an asymmetric head position, usually with a tendency to bend it to the left side. In these animals the section level suggested a possibility of some of the right red nucleus cells still functioning.

(7) Certain differences between the acute and chronic states were noticed. In the later stages there is a much greater tendency for flexed positions to be assumed, and these are often asymmetrical and sometimes flaccid and sometimes rigid. Of these rigid flexion of the terminal joints of the fore-limbs with extrusion of the claws is very common.

(8) The preparations show no sign of temperature control and never shiver. Bilateral shivering is however seen after unilateral decerebration where temperature regulation is preserved. Variations in the respiratory rate are seen after bilateral decerebration as the result of differences in body temperature, but these variations are probably not so great as in the intact animal.

(9) The respiratory rate is usually that normal for a cat, i.e., about 24. Normal respirations have been observed for days even when the section was at the lower margin of the inferior colliculi.

(10) Pseudoaffective reflexes were usually much more developed after the first few days than immediately after operation, and new responses were seen. Besides those described in the succeeding section, movements of the head away from certain noxious stimuli were noticed and occasionally a movement of the fore-limbs as though directed to the protection of the head.

(11) Vocalization was noted in ten of the 124 complete decerebra-

tions. This was rarely seen except after three or four days, and consisted most commonly in purring after the stomach had been filled with milk by a stomach tube. When purring was observed the animal was a kitten or a young female. Other cats growled, such sounds being never repeated, and in this case the sounds were only observed in old males. A true mew has only been observed in one animal which made such a sound on two occasions, but would not do so in response to nocuous stimuli. An ill co-ordinated cry, resembling the sound a cat may make while anæsthetized, has been observed in five animals, but it too is apparently sporadic and is rarely repeated.

(12) Many preparations show a well developed mastication reflex with chewing of the food (or tube), swallowing of the bolus and with a final nose and mouth-licking reflex. This may be initiated by mere opening of the mouth sometimes or by insertion of food into the back of the mouth. A stomach tube is merely swallowed during the first day, is often also chewed later, while after four or five days food may be well swallowed while a stomach tube is received with apparent objection, the head being moved about and attempts being made to spit it out.

(13) Movements are seen in animals with a section between the superior and inferior colliculi and these increase after the first few days. They consist of movements as described under (10) and (14), and also of spontaneous progression movements and of kicking when touched. They were distinct from the violent movement found with more anterior sections (already described by others). It has not so far proved possible to preserve animals for any time when the section has been at the level of the anterior border of superior colliculi, owing to the complications introduced by these violent reactions.

(14) Acoustic reflexes become more brisk after the first few days. Lifting of the head to one side (usually the left) has been often seen, and would sometimes occur in reaction to such slight sounds as were made for instance by entering the room quietly, and this in spite of the fact that the bath stirrer was maintaining a constant noise. Though the constant noise gave no reaction, it caused a reaction when the motor was started after a quiet interval.

(15) Glycosuria persisting for some time after decerebration (as described by J. Mellanby) is confirmed, but this glycosuria disappears again on the second or third day and does not reappear. The cessation of glycosuria is not caused by disappearance of glycogen.

(16) Unilateral decerebration was carried out on a series of seventeen

cats, the removal extending back to the level of the pons in some, to the anterior part of the mid-brain in others.

(17) In these semi-decerebrate animals forced movements were always directed away from the side of removal. The head was rotated with occiput away from the side of removal and the neck flexed and retracted so as to carry the head over to the sound side. In some of the more anterior removals a transient stage of forced movements to the ipsilateral side followed operation, to be succeeded invariably by the opposite.

(18) In experiments in which the semi-decerebration passed through the anterior part of the mesencephalon, extensor rigidity was found in the contralateral limbs. This was preceded sometimes by ipsilateral or bilateral extensor rigidity. When the semi-decerebration was more posterior and passed between mid-brain and pons, there was considerable variation in the rigidities and a tendency for them to be asymmetrical. The anatomical deduction is that the pathway whose interruption is responsible for extensor rigidity decussates in the mid-brain.

(19) A condition of increased resistance of the flexor muscles to passive extension was described, both in complete decerebrations and semi-decerebrations. In the latter, when the removal was anterior, this flexor rigidity appeared usually in the ipsilateral limbs, though it might be seen in the contralateral limbs for a short time after operation. Thus it alternated with extensor rigidity.

(20) Flexor rigidity as an entity may be described as tonic innervation of those muscles which are subjected to tonic inhibition during extensor rigidity. It is possible to speak of two types of decerebrate rigidity.

In conclusion we would express our thanks to Professor Sherrington for his continued help and advice throughout the course of the experiments, and to Dr. J. G. Greenfield for the hospitality extended to us in his pathological laboratory at Queen Square.

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THE PATHOGENESIS OF SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD, WITH SPECIAL REFERENCE TO ITS CONNECTION WITH ADDISON'S (PERNICIOUS) ANÆMIA, ACHLORHYDRIA AND INTESTINAL INFECTION.

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SUBACUTE combined degeneration of the spinal cord has in the past been chiefly investigated by neurologists, who were only interested in a minor degree in the associated anæmia. On the other hand, the spinal changes observed in Addison's anæmia have been investigated chiefly by physicians, whose interest was in the anæmia rather than the spinal disease. The present paper is an attempt to discuss the two groups of cases from a common standpoint, and to show that both depend upon the same underlying pathological processes—oral sepsis, absence of free hydrochloric acid from the stomach contents throughout digestion, and consequent intestinal infection and intoxication.

The term Addison's anæmia is used in this paper instead of pernicious anæmia. Addison [1] first described the disease in 1847 and called it "idiopathic anæmia." Twenty years later Biermer published his work on the same subject and called the disease "pernicious anæmia." But beyond the pernicious name he invented, Biermer added little but confusion to our knowledge of the subject, and as the disease is neither idiopathic nor necessarily pernicious, there can be no doubt that "Addison's anæmia" is the most satisfactory name.

I.—THE PATHOGENESIS OF ADDISON'S ANÆMIA AND ACHLORHYDRIA.

Before considering the pathogenesis of subacute combined degeneration of the spinal cord, it is necessary to summarize the views we hold as a result of recent investigations on Addison's anæmia, particularly with regard to its association with achlorhydria. For the following

reasons we believe that the achlorhydria is an essential predisposing cause of the anæmia.

(1) There is abundant evidence that the achlorhydria precedes the development of the anæmia. As Robert Hutchison first pointed out in 1900, there is generally a more or less long history of digestive disturbances, of the type commonly associated with achlorhydria, preceding the first symptoms of anæmia. In one case achlorhydria was actually discovered twelve, in another ten, in another three years, and in another one year before the onset of anæmia.

(2) In sixty-four out of sixty-six fractional test meals carried out at Guy's and the London Hospitals on cases of Addison's anæmia complete achlorhydria occurred throughout the period of digestion. At whatever stage in the development of the anæmia the examination is made achlorhydria is found. It was present, for example, in cases in which the hæmoglobin percentage had not fallen below 85, 85, 80 and 68; it is thus a far more constant symptom than any other, even than the hæmatological signs, such as a high colour index and the presence of megaloblasts, as these are often absent in the early stages and even temporarily when the anæmia is severe.

(3) It persists when the anæmia has almost disappeared, either spontaneously or as a result of treatment. Thus in four cases it was still present when the hæmoglobin percentage was 85, 82, 80 and 70 respectively, compared with 45, 38, 23 and 53 respectively some months or years before.

(4) There is no constant change in the curve of secretion in any form of anæmia, except Addison's. Thus fractional test meals in our last four patients with gastric or duodenal ulcer, complicated by severe secondary anæmia due to hæmorrhage, gave curves of exactly the same form as would have been expected in the absence of hæmorrhage; the percentage of hæmoglobin in these cases was 30, 33, 48 and 49, which is quite as low as one would expect to find in an average series of cases of Addison's anæmia when first examined. In two cases of secondary anæmia caused by rectal hæmorrhage with a hæmoglobin percentage of 44 and 42 respectively, and in two cases of chlorosis with a percentage of 25 and 48, the curves of gastric secretion were normal. It is obvious, therefore, that anæmia does not cause achlorhydria.

(5) In a long series of cases it becomes clear that the achlorhydria is not specific, but that whatever its origin may be, it predisposes to the development of Addison's anæmia. Bennett and Ryle [5] have shown that about 4 per cent. of normal young men have achlorhydria. The history

in many cases of Addison's anæmia points to the achlorhydria being of this congenital type. In one it was due to alcoholic gastritis, in another it resulted from a gastro-enterostomy for ulcer, and—what proves conclusively that it is primary and not secondary—in at least five cases Addison's anæmia followed the artificial achylia produced by total gastrectomy performed for cancer. There is thus no constant pathological change, such as atrophy, in the gastric mucous membrane after death, and in one case of Addison's anæmia, in which a fragment was excised during an operation for appendicitis, Dr. R. D. Passey found no atrophy and no more inflammation than in a specimen obtained under similar circumstances in a case of "benign" achlorhydria.

For the above reasons we believe that Addison's anæmia only develops in individuals who have achlorhydria. The anæmia is caused by hæmolytic toxin absorbed from the intestine, where they have been produced by the action of bacteria coming originally from the mouth, the presence of achlorhydria having deprived the stomach of its antiseptic powers, which normally exert a powerful influence in protecting the bowel from such infection.

II.—DEGENERATION OF THE SPINAL CORD IN ADDISON'S ANÆMIA.

Lichtheim [13] in 1887 described three cases of "pernicious anæmia" with spinal symptoms. A post-mortem performed on two of them showed degeneration of the posterior columns and to a less extent in the lateral columns. His clinical and pathological observations were soon confirmed by Minnich [15] and Nonne [18]; the latter author before long came to the conclusion that his original idea that the degeneration of the spinal cord was secondary to the anæmia must be incorrect and that both conditions were the result of some chronic intoxication.

In the last twenty-five years spinal cord symptoms have been recognized in Addison's anæmia with increasing frequency as they have become more systematically looked for. In 1902 McCrae [14] found them in 25 per cent. of forty cases; in 1918 Woltmann [21] found "indisputable evidence of the destruction of nervous parenchyma" in 80.6 per cent. of 150 cases, which were subjected to a detailed neurological examination at the Mayo Clinic. This corresponds closely with the figures obtained by Minnich [15] [16], who discovered degenerative changes in 77 per cent. of the spinal cords of a consecutive series of fatal cases of "pernicious anæmia."

Mitchell Clarke [17] in 1904 concluded from a study of the literature and from his own cases that the changes in the nervous system in Addison's anæmia could be clearly distinguished from subacute combined degeneration of the cord, whether or not the latter was accompanied by anæmia. We agree, however, with the view expressed by Barker [2] in 1919 that no definite line can be drawn between Addison's anæmia accompanied by changes in the spinal cord, and subacute combined degeneration of the cord accompanied by anæmia. The difference is simply one of degree, and depends upon whether a hæmolysin or a neuro-toxin is the more active. If either toxin is at first produced alone, there is more time for it to give rise to marked changes; thus when Addison's anæmia is severe and rapidly fatal, there may be no time for any nervous symptoms to develop, or, if they do develop, they may be trivial in comparison with those observed in cases in which the nervous degeneration has progressed for many months without any anæmia. There appears to be no essential difference between the clinical symptoms or the pathological changes in the spinal cord except in their severity, whether the nervous degeneration or the anæmia predominates.

III.—NATURE OF THE ANÆMIA ASSOCIATED WITH SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD.

In some of the nine cases described by Risien Russell, Batten and Collier [20] in 1900 no anæmia was present throughout the disease; in others it developed towards the end, whilst in others it was an "obtrusive symptom from the first and preceded the manifestation of nervous symptoms by many months." They definitely state that repeated examinations of the blood "failed to reveal the alterations found in pernicious anæmia," the changes being those characteristic of secondary anæmia. The red corpuscles were generally normal in shape, nucleated cells were only found in one case in very small numbers, and no megaloblasts or microblasts were present.

In 1904, Mitchell Clarke [17] from a study of five cases of spinal cord degeneration in anæmia concluded that it is by "no means only, nor even most often, that the form of anæmia is pernicious anæmia."

In an article on subacute combined degeneration of the spinal cord published in 1910, Collier [10] states that "severe secondary anæmia" is almost invariably present at some period of the disease, though its development is sometimes deferred till the last stages. But though he

regarded the anæmia as "definitely secondary," his description of the blood corresponds more closely to that of Addison's anæmia. "The colour index is usually above normal . . . Anisocytosis, poikilocytosis, and polychromatophilia are common. Normoblasts are sometimes numerous." He adds, however, that "megaloblasts have not been found, and the reaction for free iron in the liver has not been obtained in any case," but he makes the important observation that the skin not infrequently assumes a striking lemon-yellow colour.

In the same year Byrom Bramwell [7] described a case in which the nervous symptoms developed three years before the anæmia was obvious, but the blood finally presented all the typical features of Addison's anæmia. Post-mortem excess of iron was present in the liver, and there was a great increase in the red bone marrow; the spinal cord changes were typical of subacute combined degeneration. In 1915 [8] he brought forward further evidence pointing to the anæmia being of the Addisonian variety in subacute combined degeneration of the cord, even when it did not first conform to type. He quotes a case in which rapid changes occurred in the blood during the last fortnight of life, the colour index slowly rising in consecutive investigations from 0·8 to 2·3.

Single cases of subacute combined degeneration of the cord have been described by Taylor and Waterman (1903), Collins (1904), Loudon (1913), and Redwood (1920), and two cases each by Grinker (1908), and Hassin (1917), in which the anæmia was definitely of the Addisonian type. Cadwalader, describing nine cases in 1916, stated his belief that subacute combined degeneration was not associated with any form of anæmia except "pernicious" anæmia.

In his latest article on the subject, published in 1921, Collier [11] came to conclusions entirely different from those in his earlier writings. He states that a careful investigation of the blood changes at various stages of the disease and of the post-mortem findings in a large series of cases, has proved beyond any possible doubt that the blood-changes in every case are identical with those that are met with in the various stages of pernicious anæmia, and that a typical post-mortem picture of pernicious anæmia occurs frequently enough in subacute combined degeneration. In contradiction to his earlier papers he says that "megaloblasts may be found in numbers."

Addison's anæmia, particularly in the early stages and during the periods of remission, may present a blood-picture far removed from what is considered to be typical of the disease. This has been recorded fre-

quently and is the experience of all clinicians. A recent case of undoubted Addison's anæmia, in which numerous blood examinations were made and the diagnosis was confirmed post mortem, illustrates this point clearly (Table I).

TABLE I.—VARIATIONS IN COLOUR-INDEX IN A TYPICAL CASE OF ADDISON'S ANÆMIA.

Date	Red blood corpuscles per c. mm.	Hæmoglobin percentage	Colour index
22.9.21	2,200,000 ..	30 ..	0.7
8.10.21	1,500,000 ..	20 ..	0.6
1.11.21	2,800,000 ..	40 ..	0.7
11.11.21	2,400,000 ..	48 ..	1.2
18.11.21	2,088,000 ..	58 ..	1.4
5.12.21	3,100,000 ..	62 ..	1.0
20.1.22	1,600,000 ..	40 ..	1.25
10.4.22	2,400,000 ..	40 ..	0.8
15.5.22	2,240,000 ..	60 ..	1.3
12.6.22	1,640,000 ..	46 ..	1.4
26.6.22	2,440,000 ..	50 ..	1.0

TABLE II.—BLOOD EXAMINATIONS IN EIGHT CASES OF SUBACUTE COMBINED DEGENERATION OF THE CORD.

Name	Age	Date	Red cells per c. mm.	Hæmo- globin per- centage	Colour index	Poikilo- cytosis	Aniso- cytosis	Normo- blasts	Megalo- blasts	Leuco- cytes per c. mm.	Wassermann reaction
John B. ..	62	12.7.20	2,650,000	66	1.2	+	+	—	—	3,750	Negative
Wm. B. ..	73	—2.22	2,710,000	48	0.88	+	?	—	—	7,000	Negative
		27.6.22	3,200,000	85	1.3	+	+	+	—	5,090	
Thos. M. ..	65	2.3.22	3,500,000	68	0.97	+	+	—	—	9,500	Negative
		27.4.22	4,530,000	68	0.6						
		29.5.22	4,700,000	62	0.65						
		26.7.22	6,150,000	86	0.7						
Edith J. ..	40	30.3.22	3,300,000	58	0.88	—	+	—	—	7,100	Positive (G S F negative)
J. E. W. (male)	52	14.7.19	2,300,000	52	1.1	++	++	+	+	2,800	Negative
		29.7.19	1,500,000	54	1.8	++	++	+	+		
		16.9.19	3,200,000	94	1.5	?	?	+	+		
		3.3.21	3,400,000	70	1.0	+	+	+	—	6,000	
		—8.21	3,140,000	83	1.3	+	+	—	—	3,700	
Margaret H.	64	—2.22	2,860,000	85	1.5	+	+	—	—	?	Negative
Harriet G.	51	—7.22	4,710,000	56	0.6	+	+	—	—	5,800	Negative
Marion H.	42	—7.22	2,380,000	56	1.2	+	+	—	—	7,920	Negative

It would thus appear probable that many of the cases of subacute combined degeneration recorded, including the nine published by Risien

Russell, Batten and Collier in 1900, in which the blood-picture was not characteristic of Addison's anæmia, were none the less associated with Addison's anæmia. The lemon-yellow colour, which Collier observed in many cases before he came to the conclusion that the anæmia was of the "pernicious" type, is quite characteristic of the latter, and, being caused by staining of the subcutaneous fat with pigment derived from hæmoglobin, it affords just as good evidence of hæmolysis as the Prussian-blue reaction obtained in the liver and sometimes in other organs after death. This reaction, although present in almost all cases of typical Addison's anæmia, is sometimes absent in cases of subacute combined degeneration, because the blood destruction has not been sufficiently severe and prolonged.

During the time our present series of eight cases of subacute combined degeneration of the cord was under observation the blood-picture was not typical of Addison's anæmia, but it was quite compatible with an early stage of that condition, and in those cases in which repeated examinations were made the colour index was at times over one, and the film at times showed the characteristic features (Table II).

IV.—DIGESTIVE SYMPTOMS PRECEDING AND ACCOMPANYING THE NERVOUS SYMPTOMS OF SUBACUTE COMBINED DEGENERATION OF THE CORD.

In 1908 Grinker [12] drew attention to the occasional association of digestive symptoms with subacute combined degeneration of the cord and laid special stress on the frequency of diarrhœa. In 1910 Collier [10] stated that he had occasionally observed symptoms of gastro-enteritis and colitis in the disease. In the same year Farquhar Buzzard [9] stated that gastro-intestinal disturbances may precede or accompany the earliest signs of the nervous disease. In his latest contribution to the subject in 1921, Collier says that in a considerable number of cases symptoms pointing to gastro-intestinal infection, such as vomiting, diarrhœa, anorexia or constipation, were prominent before the onset of nervous symptoms.

In seven of our eight cases digestive symptoms were present. Two patients had had attacks of diarrhœa shortly before the first nervous symptoms appeared; one of these had been actually admitted into hospital on this account. In another case "bilious attacks" with occasional vomiting and attacks of flatulent dyspepsia preceded the nervous symptoms, and in a fourth there was a long history of slight

flatulent dyspepsia. In three others the digestive symptoms only appeared after the first signs of nervous disease.

The digestive symptoms, which are so frequently associated with subacute combined degeneration of the cord, are all symptoms which are often caused by achlorhydria apart from this nervous disease and apart from Addison's anæmia, and which are generally controlled without difficulty by the administration of dilute hydrochloric acid. As these symptoms frequently precede the development of the nervous manifestations, just as similar digestive symptoms frequently precede the development of Addison's anæmia, it seems probable that the achlorhydria precedes the development of the nervous symptoms. It is certainly not due to the anæmia, as the degree of this is generally slight, quite apart from the fact that it is exceedingly doubtful whether anæmia ever does give rise to achlorhydria. The fact that digestive symptoms do not always precede the development of nervous symptoms does not make it any the less likely that achlorhydria always precedes them, as the latter condition may be present for years without giving rise to the slightest indigestion, and it is indeed present in about four per cent. of normal young men without digestive symptoms.

V.—ACHLORHYDRIA IN SUBACUTE COMBINED DEGENERATION OF THE CORD.

We have had the opportunity of investigating eight cases of typical subacute combined degeneration of the cord by the fractional method of gastric analysis. In all of the eight free hydrochloric acid was completely absent throughout the period of digestion. The test was repeated in three of the cases with the same result.

So far as we know no other cases have been investigated in this way. Llewellys Barker [2] found complete achlorhydria in two cases, presumably after an ordinary one-hour test-meal. In one the anæmia at the time of the examination was said to be "quite definitely not pernicious," though the colour index was 1.1, and in the other the red corpuscles numbered 4,000,000 per cm., the hæmoglobin percentage being 90. Barker's observation is valuable confirmation of our results, but the fact that achlorhydria persists throughout digestion is of course of greater significance than the absence of free hydrochloric acid from the contents of the stomach removed in the ordinary way one hour after the meal has been taken. Dr. J. F. Wilkinson, of Melbourne, informs us that he discovered achlorhydria in a patient who consulted

him for digestive symptoms a year before the first signs of subacute combined degeneration of the cord appeared.

For purposes of control gastric analyses were made in a series of typical cases of disseminated sclerosis and tabes dorsalis. In eight consecutive cases of disseminated sclerosis achlorhydria was never found, the curves of acidity being the same as would be likely to occur in a series of eight normal people. Of nine consecutive cases of tabes dorsalis one was found to have achlorhydria; the remainder had curves which fell within normal limits, though in two cases it was somewhat high. As 4 per cent. of normal individuals have achlorhydria, the single case in this series is probably of no importance (Table III).

TABLE III.—RELATIVE FREQUENCY OF ACHLORHYDRIA IN VARIOUS CONDITIONS.

	Number of cases	Achlorhydria		Low acidity	"Normal" acidity	High acidity
		Number	Percentage			
Normal (Bennett and Ryle) [5]	100	4	4	1	87	8
Various medical diseases (Bell) [8]	425	68	16.8	58 (12.5 per cent.)	205 (45.3 per cent.)	104 (24.4 per cent.)
Addison's (pernicious) anæmia	66	64	96	1	1	0
Carcinoma of stomach	10	8	88	8	3	0
Subacute combined degeneration of cord	8	8	100	0	0	0
Tabes dorsalis	9	1	11	1	5	2
Disseminated sclerosis	8	0	0	1	7	0

Gastric analysis may therefore give information of real help in diagnosis, the presence of free hydrochloric acid in any fraction of a test-meal being probably a decisive point against the diagnosis of subacute combined degeneration, whereas the discovery of achlorhydria would considerably strengthen the probability of such a diagnosis being correct. In three recent cases, which presented features very suggestive of subacute combined degeneration, a normal curve of gastric acidity was discovered. Each eventually proved to be a case of syphilitic disease of the spinal cord. These cases are analogous with two others, the only cases in Guy's Hospital in which a diagnosis of Addison's anæmia had been made in spite of the fact that free hydrochloric acid was present in the stomach. At the post-mortem no evidence of hæmolytic was present, one being found to have infective endocarditis, and the

other, who died of lobar pneumonia, having microscopical changes in the spleen, which were typical of Hodgkin's disease.

VI.—ORAL SEPSIS.

The importance of oral sepsis in Addison's anæmia has been almost universally acknowledged since Hunter first drew attention to the subject over twenty years ago. In his article on subacute combined degeneration of the cord, published in 1910, Collier states that septic gingivitis and stomatitis are common in the disease. One of our eight patients had had all his teeth taken out on account of severe pyorrhœa shortly before we saw him. Two others had had all removed twenty or more years earlier because they were becoming loose. The remaining five had more or less severe gingivitis with pyorrhœa and septic stumps. Only one patient complained of soreness of the tongue, it was abnormally red and corrugated, but there was no ulceration. In another the tongue was abnormally smooth and shiny, the papillæ having atrophied to a great extent, although the patient, who was edentulous, was unaware that she had ever had glossitis.

VII.—THE EVIDENCE OF INTESTINAL INFECTION IN SUBACUTE COMBINED DEGENERATION OF THE CORD AND ADDISON'S ANÆMIA.

Streptococci are almost invariably present in the sockets of septic teeth, whether the individual is otherwise healthy or not, but so far as our observations go the *Streptococcus longus* is not often found in the contents of the duodenum removed during life with an Einhorn tube, except in Addison's anæmia and in subacute combined degeneration of the cord. In four normal individuals and in eight cases of infective jaundice from Gallipoli investigated by one of us (A. F. H.) with C. J. Martin in Lemnos in the autumn of 1915 no streptococci were present. Among fourteen patients suffering from various medical conditions the duodenal contents contained the *S. longus* in only three instances, one being in a patient with diabetes and slight pyorrhœa alveolaris, and the other two men with cholecystitis, one of whom also had a severe infection of his tonsils; in all three cases the gastric secretion was normal. In four of the fourteen cases achlorhydria was present, together with very severe oral sepsis in two and slight pyorrhœa in a third, but in spite of this no streptococci were found. In every one of the seven cases of Addison's anæmia and the four cases of subacute combined degeneration of the cord which we have investigated

the *S. longus* was found on microscopic examination and was obtained on cultivation of the duodenal contents. (Table IV.)

TABLE IV.—*Streptococcus longus* IN THE DUODENAL CONTENTS.

	Number of cases	<i>S. longus</i> present	Percentage
Normal	4	0	11.5
Infective jaundice	8	0	
Various medical cases	14	3	
Addison's anæmia	7	7	100
Subacute combined degeneration of the cord	4	4	

In spite of the somewhat smaller number of cases, the contrast between the 11.5 per cent. of controls, in which streptococci were found, with 100 per cent. of subacute combined degeneration of the cord and Addison's anæmia, is so striking that the conclusion can probably be drawn that an infection of the intestine with a *S. longus* is an essential factor in the production of these diseases. In any case the presence of the *S. longus* in the duodenum is evidence of active infection of the intestine. In one of our patients an autogenous vaccine made from the *S. longus* isolated from the socket of an infected tooth gave rise to a temporary aggravation of the sensation of pins and needles in the hands and feet each time it was injected.

VIII.—DISEASES OTHER THAN ADDISON'S ANÆMIA WHICH MAY BE ASSOCIATED WITH SUBACUTE COMBINED DEGENERATION.

Schultze, Nonne and Getlin are said to have reported cases of subacute combined degeneration of the cord, in which the blood picture was that of lymphatic leukæmia, and Collier refers to a similar case observed by Greenfield. I only know of two cases of lymphatic leukæmia in which a fractional test meal has been carried out. In one of these complete achlorhydria was present, but in the other the curve was normal. It is obvious that no conclusions can be drawn from the two cases, but the presence of achlorhydria in one of them would suggest that in leukæmia the oral sepsis and achlorhydria, which are the necessary conditions for the development of Addison's anæmia and subacute combined degeneration of the cord, may be present. This would explain the occurrence of cases of so-called "leukanæmia," in which the blood picture is a combination of leukæmia and Addison's anæmia, as well as those rare cases of subacute combined degeneration of the cord with leukæmia which have just been mentioned.

It is also said that severe cachexia may be associated with similar changes in the spinal cord, but we have been able to find no detailed description of such cases, the majority of which appear to have been

due to cancer of the stomach. In 30 per cent. of our cases of gastric cancer complete achlorhydria was found with the fractional test meal, and oral sepsis is of course not uncommon. Severe anæmia is more common in cancer of the stomach than in cancer elsewhere. This may be due to the fact that a hæmolytic toxin is sometimes produced when achlorhydria is present and causes a more severe anæmia than would result from the cancer toxins alone. At the same time neuro-toxins might well be produced.

Lastly, subacute combined degeneration of the cord is said to occur in connection with Addison's disease, although here again we have been unable to find any detailed reports. We have, however, had under observation a man suffering from typical Addison's disease with an extreme degree of pigmentation, a very low blood pressure, general asthenia and vomiting, in whom signs of posterior and lateral cord degeneration were present. Further investigation showed that the Addison's disease was associated with the blood changes of Addison's (pernicious) anæmia, so that the nervous changes can be regarded as a complication of the latter rather than of the suprarenal disease.

IX.—SUBACUTE COMBINED DEGENERATION OF THE CORD WITHOUT ANÆMIA.

It has generally been stated that cases of subacute combined degeneration of the cord occur without any anæmia. We have, however, seen no reports of such cases, in which blood examinations have been made during the last two or three weeks of life, and Byrom Bramwell's case, in which anæmia of a typical Addisonian form developed during the fortnight before death, shows how necessary it is to do this before concluding that the nervous disease runs its whole course without being complicated by anæmia. It would, however, not be surprising if in a small proportion of cases no anæmia occurred at all, because there is no reason why in some cases neuro-toxins might not be produced without hæmolysins, just as the latter are certainly produced in a considerable number of cases without the former.

X.—PATHOGENESIS.

In their classical account of subacute combined degeneration of the spinal cord published in 1900, Risien Russell, Batten and Collier [20] came to the conclusion that the disease is caused by some toxic agent, which is also the cause of the anæmia, with which it is generally

associated, and that it is not secondary to the anæmia. Writing ten years later, Buzzard [9] suggested that this toxin has its origin in the alimentary canal, and in 1921 Collier [11] concluded that the toxic agent responsible both for the nervous degeneration and the anæmia is of gastro-intestinal origin.

We have already given our reasons for believing that achlorhydria is an essential predisposing cause of Addison's anæmia. Our observations lead us to agree with Collier's most recent conclusion that the anæmia with which subacute combined degeneration of the cord is almost always associated is the so-called "pernicious" form, first described by Addison. It is therefore not surprising that achlorhydria appears to be present as constantly in cases in which subacute combined degeneration of the cord is the earlier and more prominent symptom, as in those in which anæmia is present alone or in which the nervous symptoms remain comparatively unimportant.

Gastric juice has two functions: it helps in the digestion of proteins, and the antiseptic action of its acid helps to protect the intestines from infection with swallowed organisms. In achlorhydria proteins pass into the duodenum in an unaltered form, and bacteria from the mouth and nasopharynx are likely to reach the intestine in far greater numbers than under normal conditions. If achlorhydria is associated with oral sepsis, secondary infection of the intestines is extremely likely to occur. The investigations of Bennett and Dodds [6] show that pancreatic secretion is also deficient in Addison's anæmia. The digestion of proteins is therefore likely to be even more deficient than in cases in which achlorhydria is present alone. Consequently in Addison's anæmia and in subacute combined degeneration of the cord intestinal infection is likely to be associated with the presence in the intestines of excess of undigested or incompletely digested protein. Under such conditions it is not surprising that toxins are produced by the bacterial destruction of proteins in abnormal quantities in the intestines. It is probable that one of these is specially toxic for the blood and leads to a hæmolytic form of anæmia, and that another is specially toxic for nervous tissues and leads to combined degeneration of the spinal cord. In most cases the former toxin is the dominant one, but in a small minority of cases the latter is the more important. Although one or other may appear to be present alone in the early stages, it is rare for the hæmolytic toxin and still more rare for the neurotoxin to continue to be produced without the other throughout the course of the illness.

XI.—TREATMENT.

The most important part of the treatment of subacute combined degeneration is to attempt to overcome the intestinal infection and so stop the development of the neurotoxic and hæmolytic poisons. Oral sepsis should be thoroughly dealt with. Every tooth which shows the slightest sign of infection on expert clinical examination should be condemned. An X-ray photograph should always be taken of all the remaining teeth, however healthy they may appear, and the slightest sign of apical infection or periodontitis should lead to their removal. In most cases every tooth will have to be extracted. If the tonsils are infected they should be enucleated, and the nose and nasal sinuses should also be examined and if necessary thoroughly treated.

The achlorhydria should be corrected by the administration of large doses of hydrochloric acid. In most cases we have found that a drachm and a half of dilute hydrochloric acid are required in order to compensate for the deficiency of gastric juice (Charts I and II). The acid should be added in the proportion of a drachm to 4 oz. of water in order to make a beverage, the acidity of which is about the same as that of gastric juice. If lemon juice and sugar are added the drink is quite palatable. It should be drunk during the course of each meal, and a little of it should be left over to sip for half an hour after the meal is completed. The patient should continue to take it without intermission for the rest of his life, as even if the intestinal infection appears to be overcome, the achlorhydria probably always remains.

Milk which has been soured with an active lactic acid bacillus should also be given for an indefinite period. Most patients can take half a pint three times a day without difficulty.

Lastly, a vaccine should be made from any streptococcus which can be isolated from the sockets of extracted teeth, from the duodenal contents withdrawn through an Einhorn tube, from the fæces and from the urine. This should be given in carefully graduated doses, beginning with very little, and slowly increasing, but it is desirable that no general reaction should follow the injections.

Unfortunately the degeneration of the spinal cord, when it has once occurred, is permanent, so that all that can be expected from adequate treatment of the intestinal infection is that the progress of the disease may be arrested. A certain amount of improvement may, however, result from a systematic course of exercises of the type that Frenkel introduced for tabetic ataxy. On the other hand, if the production of hæmolytic toxins is arrested, the blood shows spontaneous improve-

ment, and recovery can also be accelerated in severe cases by one or more transfusions of blood. Arsenic may be given, but care is necessary, as in the presence of subacute combined degeneration it is difficult to recognize the earliest symptoms of arsenical neuritis.

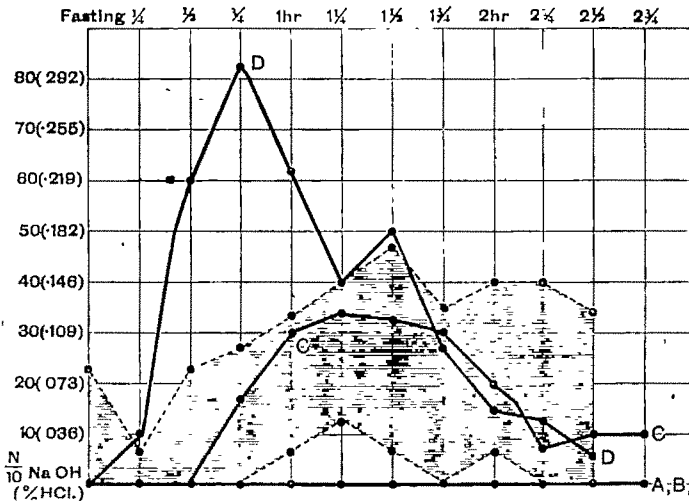


CHART I.—Fractional test meals to show free HCl in a man with subacute combined degeneration of the spinal cord. A, without addition of acid—complete achlorhydria; B, with addition of $\frac{3}{4}$ dilute HCl (B.P.) in $\frac{5}{16}$ water (=0.8% HCl) taken with the gruel and also sipped for an hour afterwards; C, with addition of $\frac{3}{4}$ dilute HCl in $\frac{5}{16}$ of water—normal curve; D, with addition of $\frac{3}{4}$ dilute HCl in $\frac{5}{16}$ water—hyperchlorhydria curve. The shaded area represents the limits for free HCl of 80% of normal people.

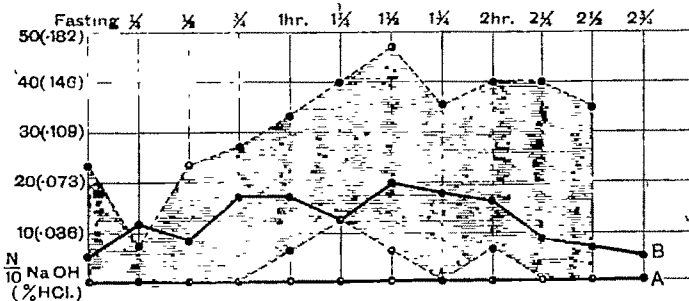


CHART II.—Fractional test-meals to show free HCl in a woman with subacute combined degeneration of the spinal cord. A, without addition of HCl—complete achlorhydria; B, with addition of $\frac{3}{4}$ dilute HCl in $\frac{5}{16}$ water.

Insufficient time has elapsed to be able to report the final result of treatment on these lines. So far it has been most promising. The anæmia, being recognized at an early stage, rapidly improves; in the two cases of our series which have been longest under observation it has

actually disappeared, and in one of these the red corpuscles now number over 5,000,000 per cubic millimetre. There has been no increase in the nervous symptoms or physical signs, and in one of the two cases just referred to the tingling of the feet and hands has almost disappeared, and the ataxic and spastic gait has greatly improved, but the physical signs are unaltered.

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'THE MENINGIOMAS (DURAL ENDOTHELIOMAS): THEIR SOURCE, AND FAVOURED SEATS OF ORIGIN.'¹

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THE tumours under consideration have long masqueraded under so many guises that it is well-nigh impossible, historically, to do them justice. In their gross appearance, they are sufficiently striking to have attracted the notice of morbid anatomists from early times, and without carrying the subject farther back than Cruveilhier we may feel assured from the admirable illustrations in his famous "Anatomie Pathologique," that he at least had encountered before 1835 some four or five examples in the course of his extensive post-mortem studies.

As these, or similar tumours, were then known occasionally to involve and absorb the adjacent bone, a lively discussion had arisen as to whether they took their origin from the diploe or dura, and if from the dura whether from its internal or external surface. Earlier writers had referred to the lesion as a *fungus duræ matris*, a term which has survived to our times; but Cruveilhier substituted for this the designation *tumeurs cancéreuses des méninges*, thereby reflecting the pathology of his day, and as late as 1858 we find R. Bennett in this country using the term *epithelial cancer* for these meningeal tumours. Such epithets as these, however, could not survive the advent of the morbid anatomist armed with the microscope and aniline dyes, nor in turn the embryologist with his classification of tissues.

In the early days of histological pathology, which had such an impetus in the 'fifties and which Sir James Paget in this country, the pupils of Johannes Müller in Germany, and Hermann Lebert, a disciple of Dupuytren, in Paris, had done so much to advance, it was customary to give descriptive designations to tumours. In 1854, in his celebrated lectures on surgical pathology, Paget confessed his inability satisfactorily to classify the large group of tumours "less malignant than cancer," to which Lebert had given the name *tumeurs fibro-plastiques*.

¹ The Cavendish Lecture, delivered before the West London Medico-Chirurgical Society, June 13, 1922.

He suggested the term *myeloid* or "marrow-like."¹ Billroth in 1856 gave the name *cylindroma* to a growth of the orbit which showed a peculiar tubular form of hyaline deposition, and at about the same time another term, still in common use for certain growths in which so-called "brain-sand" abounds, was first employed by Virchow. He had been among the first to call attention to the calcareous granules which, unrelated to any tumour growth, are found deposited in various situations in the cerebral appendages and meningeal envelopes. Though uncertain of their nature and origin, on finding these "sand-bodies" prevalent in two small dural tumours which had come to his attention, one arising from the olfactory groove and the other from the porus acusticus, he named them *psammoma*.²

Thus, names which are merely descriptive of degenerative processes of common occurrence in the tumours in question have since come to be widely employed.

At about this time there was a tendency among French writers, notably by Bouchard (1864), and by Robin [21], to substitute *epithelioma* for Lebert's "tumeur fibro-plastique," and when one considers that Robin was employing the current terminology for the lining of the serous spaces and vessels, and that he regarded the cells of the arachnoid as the source of origin of the growths, he deserves due credit for his views. This, however, was brushed aside by the greater authority of Rudolph Virchow.

In his classical "Vorlesungen" [23], though making some exceptions in regard to the psammomas, Virchow incorporated the tumours in question under the term *Sarkome der Dura mater*, and they continue for the most part to be so classified. However, in spite of their tendency to invade or absorb the bone, it came to be recognized that they were benign lesions of a peculiar histogenesis for which the designation sarcoma was inappropriate and misleading, and by the 'seventies this, in its turn, had begun to be qualified. Accordingly, such terms as

¹ In his celebrated "Anatomie Pathologique Générale," Paris, 1857 and 1861, Lebert describes and pictures as fibro-plastic tumours of the dura a few examples of these lesions, and in his "Surgical Pathology," Paget cites a most extraordinary example of a myeloid tumour which must have been a widespread bilateral and parasagittal meningioma with extensive hyperostosis cranii. The preparation is still in the Museum of St. Bartholomew's Hospital.

² Virchow came to regret the introduction (1859) of this term, because of its misuse by others. In a later article [24] he expressly states that an epithelial or endothelial tumour containing concretions is not a psammoma, that true psammomas have a connective tissue groundwork. This statement merely added to the existing confusion, though it is fair to say that psammoma bodies are apt to be more numerous in the older and more fibrous forms of meningeal tumours.

alveolar sarcoma came into use, and in France Cornil with Ranvier substituted *sarcome angiolitique* for Virchow's psammoma. But the term, sarcoma, however qualified, could not permanently survive the changing terminology of the embryologists.

Camillo Golgi, in an important article published in 1869 [14], called attention to the existing confusion in regard to these tumours. He had an opportunity to study two specimens, one of which was a typical tumour of the ethmoid region, which had come to light at autopsy in the hospital at Pavia, and he was the first to suggest the term *endothelioma* out of consideration for the employment by His of the word endothelium as opposed to epithelium. Thus, the simple term endothelioma was introduced in Italy, whence it has gradually made its way into other countries, but, unfortunately, even in the country of its birth, cumbersome word-combinations soon became attached to it. Bizzozero and Bozzolo [4], for example, soon subdivided the dural endotheliomas into three types, as *sarcoma endothelioides alveolare*, *sarcoma endothelioides fasciculatum*, and *fibroma endothelioides*, according to the manner in which the connective tissue elements behave in their relation to the endothelial cell nests, and whether endothelial or fibroblastic elements predominate. In this fashion, during the fifty years which have since passed, pathologists have vied with one another in modifying and extending the qualification "endothelial" to a wide range of tumours in a great variety of situations, in bone, thyroid, parotid, ovary, and elsewhere, into peritheliomas, hæmangio- and lymphangio-endotheliomas, and so on, with such hair-splitting refinements as to produce histological chaos.

In consequence of all this, the striking and characteristic intracranial growths we are considering, to which many of these names were first attached, have become so obscured by a multiplicity of designations that it is highly desirable to rescue and to re-assemble them under some simple caption. For this, Golgi's term, which has in later days gradually come to prevail, might suffice; but even this is now of questionable advantage, for it seems quite probable that, though attached to the dura, the tumours do not arise from this membrane proper, but rather from elements of the arachnoid which project into it; nor are they, in the parlance of some embryologists, tumours which, strictly speaking, actually originate from what are to be considered endothelial elements.

Not everyone has adopted Minot's "mesothelium" even for the cells lining the serous cavities, and it is quite evident that he had no

intention of including the meningeal spaces in this category, as some appear to have taken for granted. However, should the term be thus extended, and many anatomists so employ it, *arachnoideal mesotheliomas* would be the proper name for these tumours. But even if correct, this designation is too cumbersome for convenience, and it would seem best to sweep all these terms aside and adopt a label which is simple, and at the same time non-committal, except in so far as it indicates that the growths in question arise from the meninges. For this purpose the term *meningothelioma* was first proposed, but it has, on further consideration,¹ been shortened to *meningioma*. This word, consequently, will be used to indicate the entire group of tumours which appear to arise from the pachymeninx, whether mesothelial or fibrous elements predominate; whether the overlying bone shows hyperostosis or is unchanged; whether the growth is pedunculated or flat and widespread, and regardless of the degenerative changes and the presence or otherwise of psammoma granules.

These tumours, the meningiomas, have, as we shall see, favourite seats of origin and, though they may differ considerably in their histological picture, they are, as a rule, easily recognizable not only by their gross appearance but because of the fact that the stalk from which in their simpler form they seem to arise is so intimately incorporated with the dura that they appear to originate from it.²

¹ A note regarding the derivation of "thelium" and its combinations may not be amiss, and for the basis of what follows I am indebted to my colleague Frederick T. Lewis. The term *epithelis* (from ἐπί = upon; θήλη = the nipple) appears to have been introduced by Ruysch early in the eighteenth century, and was first used for that transitional part of the epiderm at the lips and nipple—though in time "epithelium" came to be generally used not only for the two peripheral germ layers but for the lining of the serous and vascular spaces as well. In 1865 the word *endothelium* was first used by His as a designation for the lining membrane of these cavities arising from mesenchymal cells within the middle germ layer, and the term has come into general use not only for blood-vessels and lymphatics but all serous cavities as well. Kolliker in 1882 had used the term *mesepithelium* for the lining of the body cavities and urogenital epithelium, reserving the term endothelium for the vessels, synovial cavities, meninges, and so on; and to the same tissues Minot a few years later gave the name *mesothelium*. All three terms, *epi-*, *endo-*, and *mesothelium*, would appear to be unfortunate in view of their derivation in part from θήλη, but they, nevertheless, have come to convey an idea.

² There are a few tumours which possibly are allied to the meningiomas, but which have no dural connection: they appear to arise from the pia. They are rare tumours of an angiomatous nature, whereas those under discussion are relatively non-vascular. Another still more rare tumour (particularly so in man) is the so-called cholesteatoma of the choroid plexus. It is actually an endothelioma with extensive psammoma deposit, and is often bilateral.

INCIDENCE.

Some years ago all of the material relating to the several meningiomas, intraspinal as well as intracranial, then included in my tumour series, was gathered with the intent of publishing in detail our clinical and operative experiences with these interesting lesions. This project, however, was interrupted by the discovery that the acoustic tumours (neurinomas of Verocay), which in several instances had been diagnosed as fibro-endotheliomas, were distinctive tumours of an entirely different order. The "endotheliomas" were consequently dropped for the time being, in order to make a more thorough study of the tumours originating from the eighth cranial nerve, commonly described, in view of their location, as tumours of the cerebello-pontile angle.

In a monograph ultimately published on the subject of the acoustic tumours [8] it was pointed out that these lesions when bilateral are not infrequently accompanied by multiple small meningeal endotheliomas, so that tumours of these two types (neurinoma and meningioma) are in certain respects related. Nevertheless, it is far more usual for one or the other to occur in isolated form, and until something more is learned of a common ætiological factor it is undoubtedly best to consider them apart and as distinctive lesions.

The time has long since passed when we could hope to advance our knowledge of intracranial tumours to any great extent by considering them as a whole. Even their mechanical or pressure effects, which might be expected to be more or less similar in all cases because of the rigid character of the bony chamber within which they arise, differ widely, and it is notably true of these meningiomas that they may attain a huge size without giving rise to any of the so-called cardinal symptoms of tumour, notably headaches and objective changes in the eye-grounds.

Intracranial tumours, indeed, are so protean in form; they behave in such different ways; they provoke such varied clinical pictures; and the proper method of dealing with many of them, even when they are exposed by an operation, is in many cases still so problematical, that our only hope for progress is to particularize on certain groups of cases.

There are three ways in which a large material such as is before us may be profitably attacked. We may (1) concentrate our attention upon tumours of certain histogenetic types whatever their situation; (2) we may study tumours of all types in a given situation; or (3) what is perhaps better still, we may restrict our analysis, as was done with the acoustic tumours, to tumours of a single type in a given situation.

Only by the adoption of one of these methods can one's casual acquaintance with a disorder, made at the bedside or operating table, ripen into familiarity. Each has its advantages, but for the purposes of this particular study I shall adopt the first, and consider the meningiomas as a whole.

VERIFIED MENINGIOMAS.

On various occasions an explanation has been given of the system under which the tumour cases of my clinic are classified. They are listed as (1) *tumour verified*, when the character of the lesion has been histologically determined at operation or autopsy; as (2) *tumour unverified*, when the presence of a growth is reasonably certain or, indeed, when it may actually have been seen but without removal of a fragment for verification; and as (3) *tumour suspect* to include those cases referred to the clinic with a presumptive diagnosis of tumour, of the justification of which there remains considerable doubt.

In our present connection we are interested only in the 751 verified intracranial tumours, and without going into the detail, unnecessary for our present purposes, of distinguishing between the various sub-varieties of gliomas, adenomas, and so on, the cases may be tabulated as follows, in order to indicate the ratio of the meningiomas to other main tumour groups.

TABLE OF VERIFIED INTRACRANIAL TUMOURS TO MARCH 15, 1922.

Gliomas	314 cases (41·8 per cent.)
Adenomas (chiefly pituitary)	159 „ (21·2 „)
Meningiomas	85 „ (11·3 „)
Neurinomas (acoustic)	63 „ (8·4 „)
Congenital tumours	40 „ (5·3 „)
(a) Suprasellar tumours (chiefly of pharyngeal pouch origin)	28
(b) Cholesteatomas, dermoids, and teratomas	12
Granulomas	33 cases (4·4 per cent.)
(a) Gummas	12
(b) Tubercles	21
Papillomas (choroid plexus)	11 cases (1·5 per cent.)
Angiomas	7 „ (0·9 „)
Metastatic and invasive	27 „ (3·6 „)
Miscellaneous and unclassified	12 „ (1·6 „)
	751

The meningiomas, as can be seen, stand in about a one-to-four ratio to the gliomas or brain tumours proper, and if we add to this intracranial group of eighty-five cases twelve others which have arisen in

the spinal canal, there are, at the time of writing, nearly 100 tumours to deal with.

Anything like a complete analysis of these cases would far exceed the possibilities of a single address if the innumerable questions which would naturally arise were answered with any measure of completeness. The interest of the physician and neurologist would centre on the symptomatology and diagnosis—particularly upon the mistakes in diagnosis, and in these the psychiatrist, for reasons to be pointed out, is concerned perhaps more than any other. In the province of the ophthalmologist lie the visual field distortions, the examples of unilateral exophthalmos, and, above all, the changes—or what is possibly more important, the lack of changes—in the eye-grounds, for a choked disc may be absent or at least long delayed; on the other hand, in the suprasellar lesions a primary optic atrophy may be the essential guide to the site of the lesion. Some of the tumours originate near the porus acusticus with loss of hearing as an early symptom, and so concern the otologist. Others which arise from the olfactory groove and invade the ethmoid cells come into the province of the rhinologist, and that newest of specialists, the endocrinologist, doubtless may have difficulty in distinguishing primary pituitary disease from the dyspituitarism secondary to one of these growths which so commonly arise from the meninges bridging the sella. And, last of all, the interests of the surgeon are focused on the methods employed for the removal, particularly of the more inaccessible of these tumours, and upon the end results which may be obtained. Being one of them myself, the temptation is strong to yield to the desires of my own kind, and yet, in view of the very seriousness of his therapeutic measures, it behoves the surgeon, even more than others, to know all that he can learn regarding the origin, site, and characteristics of the lesion he plans to attack before he goes into action. I propose, therefore, though it is a somewhat less exciting story, to confine myself on this occasion largely to the two points mentioned in my title—the source, and the seats of predilection of the meningiomas.

THE SOURCE OF THE TUMOURS.

In 1911 an opportunity was afforded for an enlightening post-mortem study of one of these growths which had been undisturbed by previous operative manipulations. Including three spinal tumours, it was the fifteenth case in the series, and we were then still labouring under the impression that the growths took origin from the dura and were of

various kinds. Most of the preceding tumours had possessed a broad base of meningeal attachment, and until this case no particular attention had been paid to the meninges remote from the lesion, except to note the presence of multiple herniations which had early aroused our interest.



FIG. 1.--Fragment of calvarium overlying point of origin of tumour, showing slight invasion of inner table without hyperostosis. (Arrows show groove of sinus sagittalis.)

The patient, a woman aged 41, was admitted to the John Hopkins Hospital in a profound stupor, obviously in the terminal stage of compression from a brain tumour. An incomplete story was secured from a relative, of headaches for many years, of five months' confinement in bed with increasing disability of her left side, of progressive mental impairment, and finally of somnolence. She succumbed twenty-four hours after a first-stage osteoplastic procedure, at which time the dura was not opened. Had her condition at this first session justified a more prolonged exploration with exposure of the brain, the tumour would in all probability not have been disclosed, in view of its small surface area confined to the mesial edge of the hemisphere.

As is our custom at autopsy when circumstances permit, the brain was fixed before removal by a formalin perfusion through the carotids in order to preserve the pre-existing distortions which are otherwise considerably modified. On removal of the calvarium there was disclosed, about 5 cm. anterior to the Rolandic point, a small area (fig. 1) overlapping the groove of the

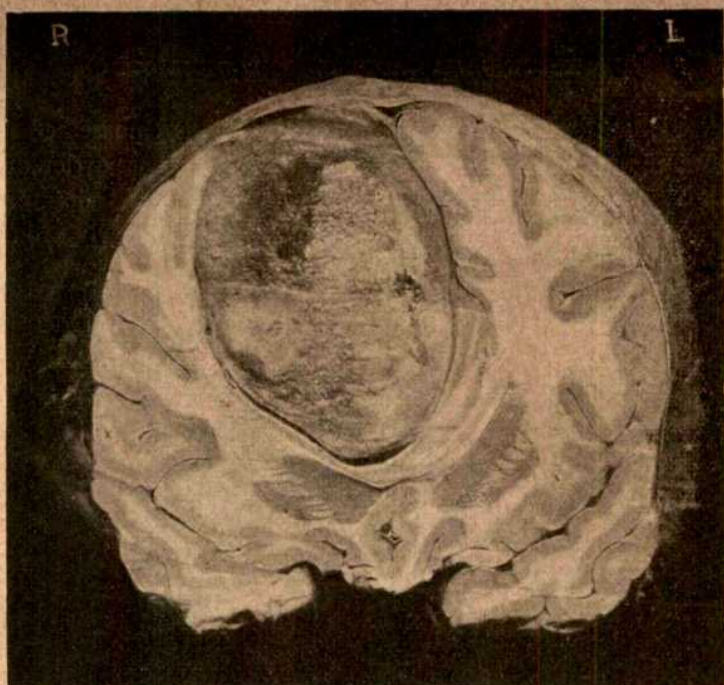


FIG. 2.—Coronal section through tumour, viewed from before, showing great dislocation of falx and corpus callosum.

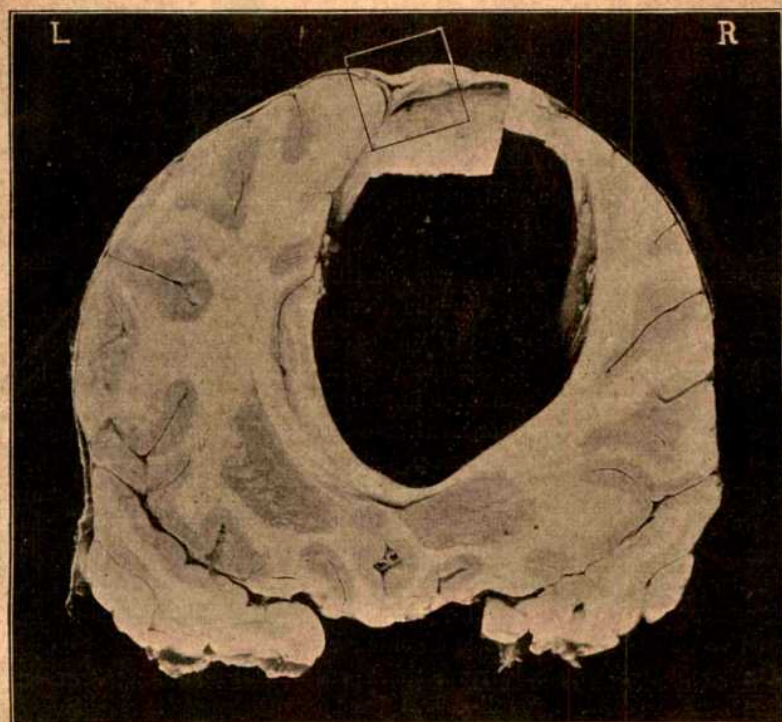


FIG. 3.—Coronal section viewed from behind, showing cavity occupied by the tumour and its only point of attachment under the lateral expansion of the sinus and at the angle of the falx.

sagittal sinus where the dura was adherent. The brain was removed, so far as possible, with its dural envelope intact, and a coronal section, through the point where the adhesions had been noted, transected a large tumour (fig. 2), of about 150 gm. weight, which had greatly deformed the hemisphere, and practically obliterated the ventricles. Except for the small stalk, from which the growth evidently arose, situated in the parasagittal angle and underlying the parasinoidal expansion of the sinus, the tumour was nowhere adherent (fig. 3). Hence, though apparently within, it actually lay outside of the hemisphere, whose pial covering remained intact over the deformed convolutions.

Microscopic sections through the point of meningeal attachment showed (fig. 4) that the tumour had invaded the sinus without thrombosing it, and though traces of the intervening dura still remained, it had been so effectually destroyed that to regard the sinus wall as the starting-point of the growth was an inevitable conclusion.

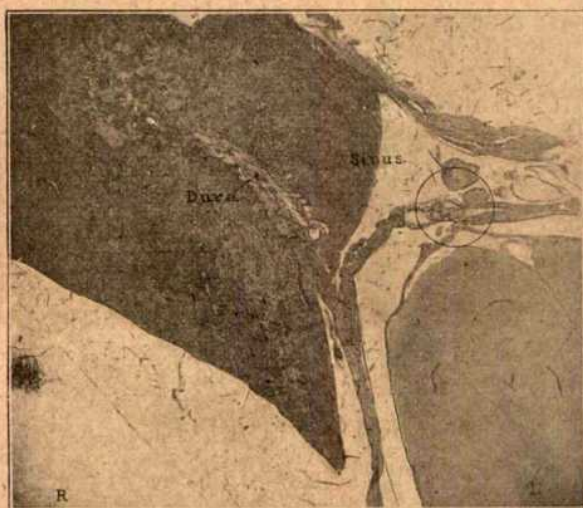


FIG. 4.—Section from area of attachment (squared area of fig. 3), showing invasion of sinus by tumour on right, and on left the arachnoid villi and cell clusters.

The lesion itself presented in different areas a most varied appearance. In some areas (fig. 5) it had a fibromyxomatous appearance, but for the most part (fig. 6) there were masses of endothelial cells with a more or less well-marked alveolar arrangement surrounded by bands of fibrous tissue, the cells of which in some places formed large fibrous whorls. Many areas showed extensive hyaline degeneration, and psammoma bodies together with so-called corpora amylacea were in abundance.

There is nothing unusual in the foregoing description of this particular tumour, for which a variety of names might be used. It

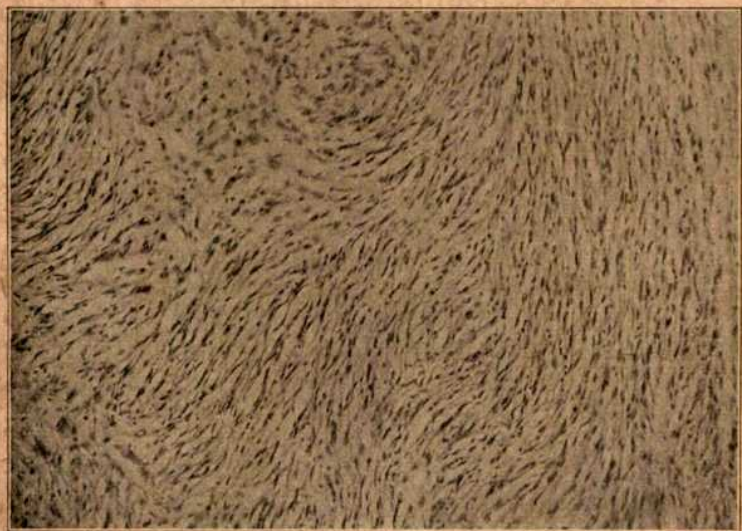


FIG. 5.—Fibromyxomatous area (mag. $\times 100$).

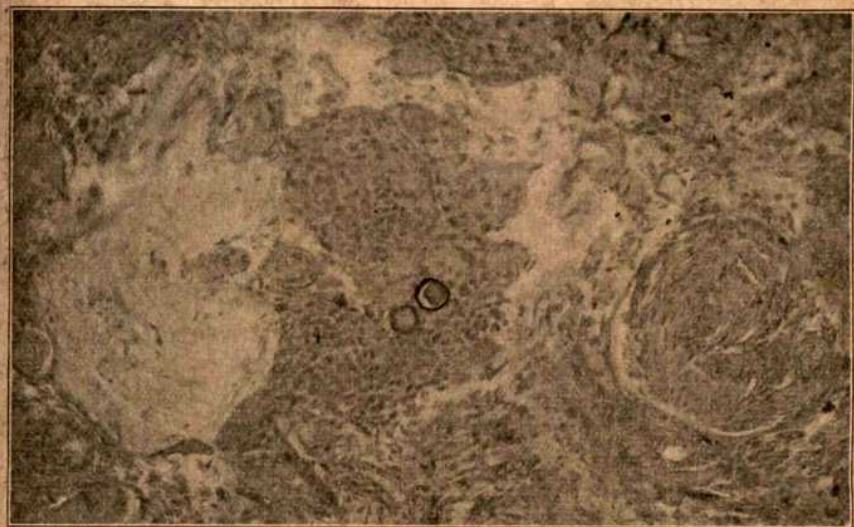


FIG. 6.—Endothelial cell alveolae with fibrous whorls, psammoma bodies and hyaline areas (mag. $\times 100$).

would probably deserve the term fibro-myxo-endothelio-sarcoma, and its seeming invasion of dura and bone would justify the assumption that it had malignant qualities which in time might have produced metastases. The whole story is essentially commonplace, and tumours of corresponding nature, beyond enumeration, have from time to time been reported in the literature.

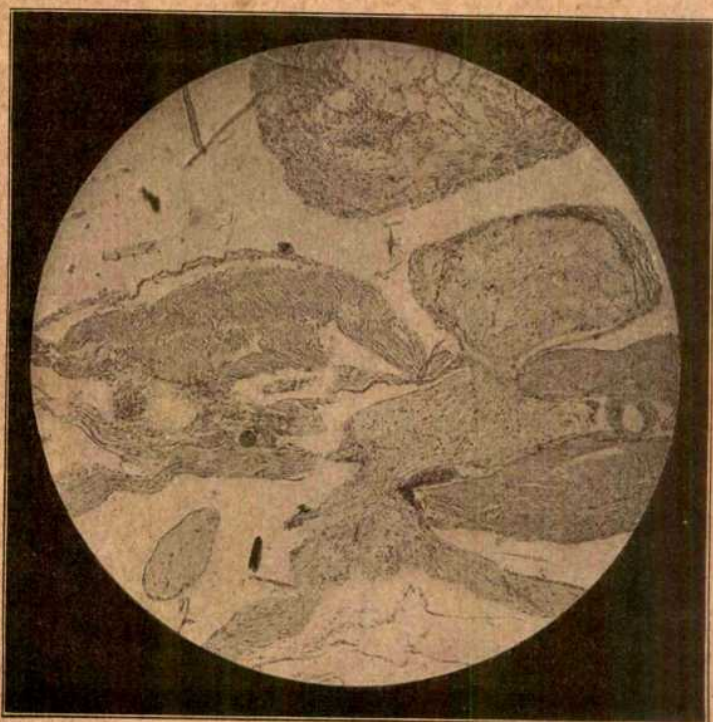


FIG. 7.—Showing an arachnoid villus projecting through dura into sinus. Also nests of arachnoid cells and psammoma body lying within dura. (Area circled in fig. 4.)

But something apart from all this, of importance in our present connection, was observed in the meninges remote from the tumour. As already mentioned, the brain after fixation¹ had been removed with its

¹ A word in regard to this may not be amiss, for I believe that nothing has served to further our understanding of the mechanical effects of tumours so much as the abandonment of the time-honoured method of handling and sectioning the unhardened brain at autopsy after removing the calvarium and stripping off the dura. This unfortunate procedure, which is still an habitual one, has done much to delay our knowledge, particularly of the secondary disorders in cases of brain tumour which concern the cerebrospinal fluid pathway in ventricles, cysternæ and leptomeninges. For not only is the tumour topography largely altered if fluid escapes before the tissue has been fixed, but with the meninges stripped from the brain there has been little incentive in the past to study them in their relation to the adjacent cortex.

meninges largely intact, and sections through the unusually small stalk of the tumour gave a definite clue to the histogenesis of the lesion. Projecting into the sinus on the side of the uninvolved hemisphere were a number of hypertrophied arachnoid villi (fig. 7), capped by clusters of endothelial cells of precisely the same character and staining reactions as those of the alveolated masses of cells comprising the bulk of the tumour. Many of these cell-clusters disclosed in the dura showed a tendency to the familiar whorl formation (fig. 8), and in association with them were psammoma bodies in considerable numbers,



FIG. 8.—Showing typical cluster of arachnoid cells arranged in whorls and lying within dural layers remote from tumour.

In short, scattered through the uninvolved and presumably normal meninges were all the elements characterizing the tumour proper, these elements being of arachnoidal rather than of dural origin, though encased within the latter membrane.

This observation, so enlightening to us eleven years ago, proved, as will be seen, to be by no means an original one. It gave us, nevertheless, a new conception of the possible source of origin of these interesting tumours and suggested studies in two directions, the first of which might not have been so vigorously pursued had we then been

aware that our views were far from being novel. We undertook, on the one hand, a detailed study of the meninges in areas distant from the tumour in all similar meningeal growths; on the other hand, we began to investigate the arachnoid villi, and this in due course led us into a consideration of the cerebrospinal fluid circulation as a whole.

During the first two years after my transfer in 1912 to Boston, these studies, which had been started in the Hunterian Laboratory at the Johns Hopkins some time before, were continued in collaboration with Lewis H. Weed in the Laboratory of Surgical Research at Harvard, and due largely to his unusual gifts as an investigator considerable progress was made. In the series of papers which were published in 1914 [10], special attention was paid to the arachnoid villi whose function as points of escape for the fluid from the arachnoid spaces into the dural sinuses, though previously surmised, Weed, for the first time I believe, conclusively demonstrated.¹ The villi, in short, appeared to us to play a far more important physiological rôle than had been commonly ascribed to them. But before considering further this aspect of the subject and its bearings upon the tumour question, it is proper to make due acknowledgment to at least three authors by whom our views regarding the origin of these tumours proved to have been anticipated. It is not at all unlikely that there may have been others who have expressed similar ideas in papers under obscure titles which have not come to my attention.

In a brief article published in 1864, John Cleland [7], late Professor of Anatomy in Glasgow, set forth with prescience, the more remarkable when one considers the source of his material for study, the view that two tumours which he had found in the dissecting room, one of them arising from the cribriform plate and the other from the right frontal region adjacent to the superior longitudinal sinus, took their origin from the arachnoid rather than the dura. He observed that in structure they resembled the Pacchionian granulations in a number of points: that connective tissue bands ran through them, that concretions were present in both tumours, and new bone formation in one of them. In pointing out the proximity of these tumours to the falx, he mentioned the bony plaques often found attached to this membrane, and in agree-

¹ On his return to Baltimore, Weed's further pursuit of these investigations led, among other papers, to the publication of his monograph ("The Development of the Cerebrospinal Spaces in Pig and Man." Contributions to Embryology, No. 14. Carnegie Institution of Washington, Publication 225, 1917) on the development of the arachnoid, which represents the most important advance in our knowledge of the meninges since the classical work of Key and Retzius.

ment with Rokitansky attributed them also to the arachnoid rather than to the dura. Similarly, Ch. Robin [21] in France, described in 1869 two tumours likewise met with in the dissecting room. He also attributed them to the arachnoid, and in a long and scholarly article made a strong plea for their epithelial origin.

In another more extensive study published ten years before our interest in the matter was first awakened, Martin B. Schmidt, of Zürich [22], likewise called attention to the probable relation of the Pacchionian granulations to the so-called sarcomas and psammomas of the dura. In the course of his post-mortem examinations Schmidt had chanced to encounter twelve small meningeal tumours which he made the subject of special study. He was led to make a thorough histological survey of the meninges, and gave the first clear description of the microscopic islands of endothelial cells (Zellzapfen) which are found between the layers of the dura, in numbers which increase with advancing age in practically all individuals.¹ He recognized that these cell masses are related to the arachnoid tufts or villi, that they are themselves unquestionably of arachnoid origin, that they have certain seats of predilection, and, inasmuch as the cells comprising them were identical with those in the small tumours he had studied, he came to the same conclusion that Cleland and Robin, on less sufficient evidence, had reached years before, that they were the starting-point of these growths which, therefore, strictly speaking, have a leptomeningeal rather than pachymeningeal origin.

In medicine perhaps more than in other walks, discoveries are constantly being re-made and views being readvanced, for knowledge spreads slowly and facts once known and recorded are easily overlooked or forgotten. In 1915, in the last of our series of papers on the cerebrospinal fluid and its pathway, a paper chiefly devoted to the calcareous and osseous deposits associated with a cellular hyperplasia of the arachnoid [11], we in turn put forward as novel precisely the same views Cleland had advanced fifty years before regarding the derivation of these tumours from the arachnoid cell clusters. Five

¹Others had observed these cell masses before Schmidt. They had possibly been seen long before by Rainey [20], who imagined them to be ganglionic structures which regulated the blood supply of the cerebral vessels. Fifteen years later Ludwig Meyer [18] [19] in a more accurate study of the meninges in cases of dementia referred to them as "epithelial granulations." Meyer recognized their relation to the arachnoid, noted the calcareous deposits which Virchow later named, and pointed out the relation of these cell clusters to the bodies of Pacchioni, which Luschka [16] a few years before had conclusively shown to be of arachnoid origin.

years later, Mallory [17] re-advanced the same views, and designated the tumours with the histological aspects of which he was chiefly concerned, as *arachnoid fibroblastomas*. Weed in the same year, though more interested in the physiological rôle of the membrane as a fluid container, nevertheless presented a convincing series of pictures from the meninges of the cat, showing that the clusters of cells may range from a moderate hypertrophy to actual tumours, in which most of the characteristic degenerative changes of these growths, as met with in man, occur.

MULTIPLE CEREBRAL HERNIATIONS.

There is another matter relating to the arachnoid villi, apart from their histological characteristics and their possible relation to tumours, which had engaged the attention of a few pathologists. In 1870, before the Würtzburger Medical Society, von Recklinghausen exhibited as a curiosity a brain from a case of cerebral tumour in which small bits of cerebral substance, projecting into minute openings of the dura, more especially over the temporal lobe, had been torn off in the course of its removal. These minute lesions he recognized as multiple hernias of the cerebral substance. They had been observed by others long before him, by Cruveilhier for example, but no particular significance had been attached to them.

The matter excited no great interest until twenty years later when Benecke [2] reported as a great rarity two further cases showing these herniations, which he attributed to pressure. He pointed out that nests of endothelial cells were invariably present somewhere on the surface of the minute cerebral protrusions, and this led him to recognize their relation to the Pacchionian granulations.

Though in 1901 four other cases were incidentally recorded by Blasius [6] from Benecke's laboratory, the first thorough study of these lesions was published in 1908 by S. Burt Wolbach [28] who had observed them in a series of cases in which there had been tension, not, however, always due to tumour. Wolbach emphasized what is important in our present connection that the herniations occur in the regions where the normal arachnoid villi abound, a fact which carries with it the implication that the dural venous sinuses and their main branches are to be found in the same situations. He showed, furthermore, as did Schmidt, that these are microscopic or what one might call potential Pacchionian granulations, and concluded that "the multiple hernias of cerebrum and cerebellum always enter the dura through fissures occupied by arachnoid villi."

Though Schmidt himself published nothing further on the subject of the *Zellzapfen*, his interest evidently did not lag, for at least two papers, bearing on these matters, appear to have emanated from his laboratory. The first of them by Sophie Wojno [27] was on this subject of cerebral herniations which she recognized as occurring in the villi; but she dwelt chiefly on the fact that they may be found in conditions unrelated to tumour and attributed them, it would seem, to defects in the pia subjacent to the villi, which thereby permit the herniations to take place.

It may be recalled that all but one of the twelve meningiomas Schmidt had described were small growths and accidental post-mortem findings. Nevertheless, even under these conditions he had observed some of these herniations, more especially in the middle cerebral fossa. Apparently, therefore, he and his pupil were on the look-out for some explanation for them other than tension. They consequently were regarded as "physiological" herniations rather than pressure phenomena, and were attributed by Wojno to leptomeningeal defects.

There is, it seems to me, a much more plausible explanation of the presence of these herniations when there is no demonstrable increase of intracranial tension—a matter indeed very difficult to gauge by post-mortem appearances alone. In view of what we now know of the ease with which the brain takes up fluid and becomes oedematous, there are probably few individuals who with advancing years escape from periods of increased intracranial tension due to one cause or another. These must be particularly common in association with arterio-vascular disorders, and it is easily conceivable that the arachnoid villi under these circumstances may not only become hypertrophied into visible Pacchionian granulations, but that actual herniations may occur and subsequently recede with the subsidence of the oedema. Even in the presence of tumour when intracranial pressure is relieved by withdrawal of cerebrospinal fluid, by the intravenous administration of hypertonic salt solution, or more permanently by a generous decompression, it is not unlikely that these minute hernias may become reduced just as may the large hernias which protrude through operative defects in the skull. An illustration of this in the process of taking place is shown in the accompanying figure (fig. 9). The condition came to light during the study of the meninges of a patient who had been operated upon over the cerebrum through an error in diagnosis, when in reality there was a cerebellar tumour with internal hydrocephalus and great tension. A cerebrospinal leak communicating with

the ventricle occurred, and fatal meningitis was the result, but for the few days before death there was a complete release from the pre-existing supernormal tension; and at autopsy it was evident even to the naked eye that many of the large and multiple hernias which abounded were being withdrawn from their pockets in the arachnoid.

These minute herniations, as a matter of fact, are very commonly produced by long-continued states of increased pressure. That they project into and dilate pre-existing spaces there can be no doubt, and that these spaces communicate with the arachnoid is evident from the

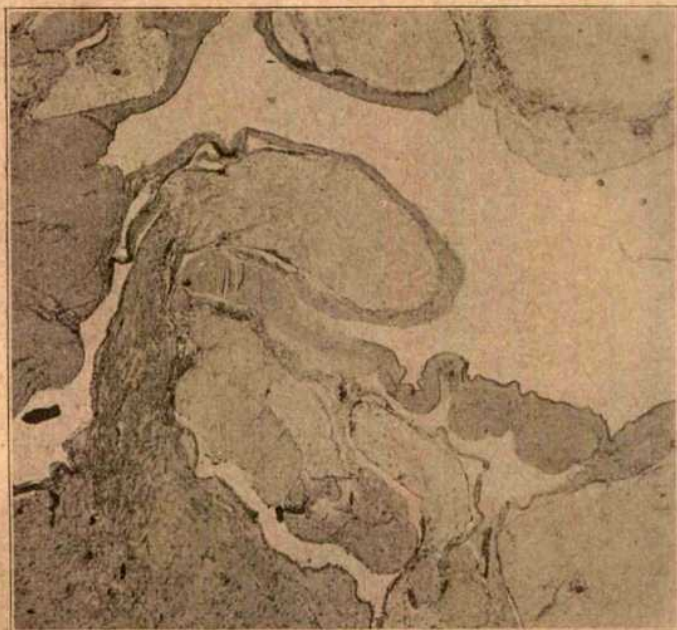


FIG. 9.—A cerebral hernia in the process of withdrawal from an arachnoid villus.

character of the cells lining them. What interests us chiefly at this time are the areas in which they are most commonly observed, since they betray the situations of the chief arachnoid villi and their associated cell-clusters. They abound, as might be surmised, along the major dural sinuses where the tentorium and falx unite with the dura over the cerebral and cerebellar convexities, but they are also to be found in the basal meninges, being especially common over the tips of the temporal lobes and in the region of the Gasserian ganglia, where they correspond likewise with the situation of the venous sinuses. They can be best studied in previously hardened brains removed with their

envelopes so far as possible intact; the accompanying figure (fig. 10), in which the relation of the protrusions to the branches of the vasa meningea media is apparent, gives an illustration of their distribution over the convexity.

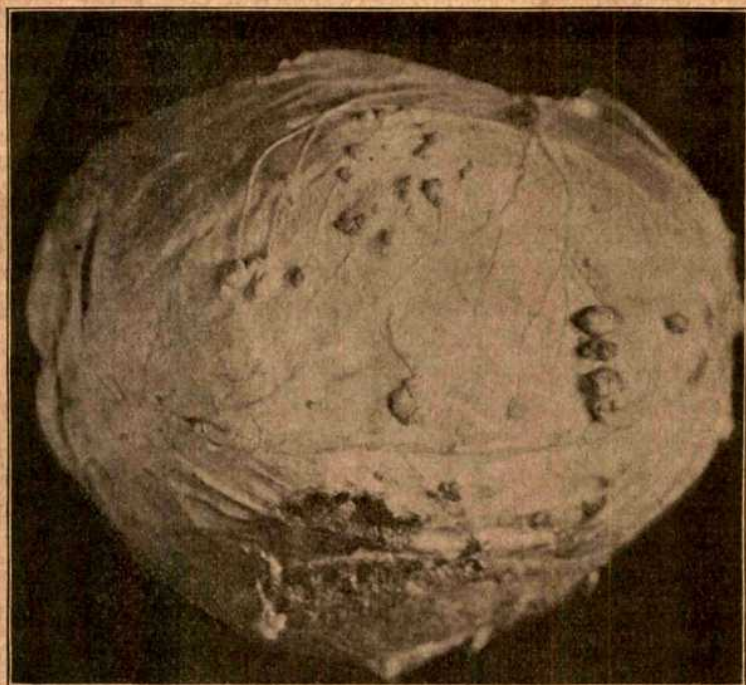


FIG. 10.—Showing multiple herniations, projecting through the dura over the left hemisphere, produced by pressure due to a large suprasellar endothelioma.

ÆTIOLOGY.

Why should these cell-clusters in the arachnoid have a tendency in middle life to undergo tumefaction? An answer to this question, owing to the many and wide gaps in our knowledge, must be essentially speculative. However, some approach to it can be made. As in other tumours, the more obvious factors are age, congenital predisposition, trauma and physiological activity. Schmidt's original observation that the cell-clusters are absent or difficult to demonstrate in infancy and become more pronounced with increasing age, has been confirmed by others. In this connection the age of the ninety-seven patients with meningiomas, as recorded at the time of their admission to hospital, fall in the successive decades as follows :—

0—10	..	..	..	0	50—60	..	..	..	21
10—20	..	..	..	9	60—70	..	..	..	10
20—30	..	..	..	11	70—80	..	..	..	0
30—40	..	..	..	23	80—90	..	..	..	1
40—50	..	..	..	28					

These figures naturally represent the age when symptoms had become pronounced, and probably an average of five or ten years should be subtracted if one were to estimate the age of onset. Nevertheless it can be seen that these tumours, unlike the gliomas, are rare in the first two decades, and reach their maximum in the fifth, a decade at least later than the period of maximal frequency for the pituitary adenomas and the acoustic tumours.

The fact that in cases of neurofibromatosis (Recklinghausen's disease), multiple meningiomas occasionally co-exist with multiple neuromas of the cranial nerves, suggests that some congenital fault may be responsible. However, they occur singly with far greater frequency. Curiously enough, they bear unmistakably a close relation to trauma of one sort or another¹. In so many of the cases in the series has a tumour been found at the exact situation where a stunning blow had been received on the skull years before, that this must represent something more than mere coincidence. On the circumstantial evidence it is tempting to assume that the injury has bruised the meninges and caused an extravasation, to aid in the absorption of which the local cell-clusters have been incited into a state of morbid activity. It is not improbable, too, as emphasized by Borst, that some form of injury other than a blow may serve to incite a pachymeningeal reaction and lead to tumour growth. In one of the cases included in the series, an unsuspected frontal endothelioma was found post mortem associated with a subjacent chronic abscess. Moreover, psammomas and endotheliomas have been observed by Berger [3], Dufour [12], Henschen [15], and probably by others, in connection with old cases of healed spinal tuberculosis in which there were unmistakable evidences of pachymeningitis. Henschen, in particular, lays great stress on this relationship in reporting a case which showed multiple tumours. They have been observed, too, in association with pachymeningitis interna hæmorrhagica. In explanation of all this it must be borne in mind that the cells which line the arachnoid actually represent an organ of great

¹ The youngest case in the series, for example, a boy of 13, with a 100-grm. meningioma which originated from the lower margin of the falx, had had symptoms for five years. He had received at birth an extensive cranial injury, associated in all probability with a tear of the falciform membrane.

functional potentialities. It is here that the studies of L. H. Weed and his co-workers have thrown a guiding light on the subject, 'for though an anatomist, Weed's interests have been on the side of function rather than structure.

To state the matter briefly, the arachnoid villi in close association with which the cell-clusters abound, act as organic filters interposed in the pathway of the cerebrospinal fluid, between the subarachnoid spaces and the dural sinuses. Their non-development or their occlusion by foreign particles, whether the product of injury or disease, or suspensions of substances such as lamp-black introduced artificially into the cerebrospinal fluid, will lead to stasis of the fluid and hydrocephalus, provided the occlusions are sufficiently widespread [26].

Furthermore, the cell-clusters under the stimulus of these injuries are prone to hypertrophic enlargement. It has been shown by Essick [13] that when the villi are experimentally blocked by particulate matter, whether sterile or the product of inflammatory reaction, the arachnoid cells proliferate abundantly, take on the function of phagocytes, and even become free-moving macrophages in the subarachnoid spaces. We may regard these cells, therefore, as agents which play a rôle in keeping the points of outlet of the fluid free from the mechanical obstructions produced by debris.

It is conceivable, therefore, that with advancing years the mesothelial cells comprising the cell-clusters are called upon from time to time to undergo periods of increased functional activity in their phagocytic rôle, after which they remain permanently hypertrophic or subsequently undergo the characteristic and well-known degenerative changes to which they seem predisposed. Hence their apparent increase in size and number with advancing age. On the other hand, some of the cell-clusters, possibly in consequence of these periods of activation, show neoplastic tendencies under certain circumstances obscurely related to the genesis of tumour formation in general.

THE SITUATION OF THE TUMOURS.

It is evident from what has gone before, that at least four observers between 1864 and 1920 have independently come to the conclusion that these tumours, herein called meningiomas, are derived from the arachnoid cell-clusters. The relation of these groups of mesothelial cells to the functioning villi and of the villi to the dural venous sinuses, has been emphasized. It has been shown further that the

places where the villi abound is indicated by the distribution of the minute cerebral hernias which protrude into them in cases of marked intracranial tension. It remains to be seen whether there is any definite correspondence between these regions and the points of origin of the tumours themselves.

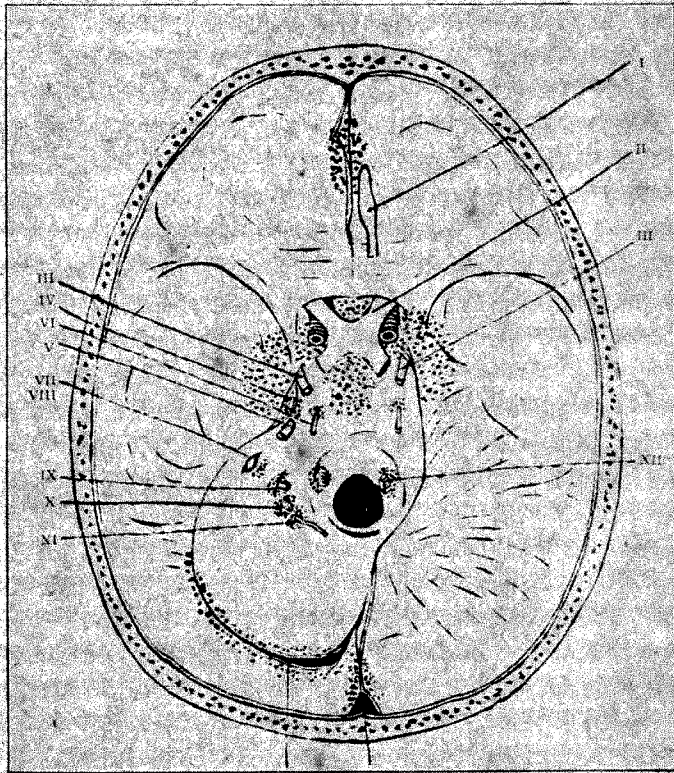


FIG. 11.—From Aoyagi and Kyuno, showing the situations of the cell clusters.

The only paper on this subject, to my knowledge, was published in 1912 by Aoyagi and Kyuno [1] and for a translation from the Japanese I am indebted to Professor Tanaka, of Okayama. These authors made studies of the dura of individuals of various ages to determine the seats of predilection of the arachnoid cell-clusters, and identified their presence in the following situations (fig. 11), viz., along the sinus sagittalis superior; near the crista galli; the sinus transversus; surrounding N. oculomotorius, trochlearis, abducens, and trigeminus; around the hypophysis; near the sella turcica; the plexus basilaris; at

the point of penetration of the dura by the third, seventh, ninth, tenth, eleventh and twelfth cerebral nerves; and also at the points of penetration of the nerve-roots of the cervical spine.

Furthermore, they gathered from the literature thirty-six cases of so-called dural tumour (variously termed sarcoma, psammoma, endothelioma, sarcomatous endothelioma, spindle-cell sarcoma, &c.) and added three cases of their own, all evidently "meningiomas." The situations in which these thirty-nine tumours were reported corresponded sufficiently well with the principal locations of the cell-clusters to justify the conclusion that all the tumours—endotheliomas, psammomas and sarcomas alike—arose from these bodies.

For the purpose of this lecture, the accompanying drawings have been made, with as great accuracy as our records of operations and the study of autopsy material permits, to indicate the areas of dural attachment of the meningiomas in my personal series. It must be admitted that in certain cases it may be difficult, even with the material in one's hand, to judge of the exact point of origin of a meningioma. This is particularly true of the spreading flat tumours¹, for such a small stalk of attachment as appears in the case herein recorded in some detail (figs. 2 and 3) is unusual even in the large potato-like growths which tend to be more or less pedunculated.

The meningiomas, in short, may be divided into two general classes: the large growths, often more or less irregularly lobulated, which incline on the whole toward a spherical form, and the tumours *en plaque* which are but slightly elevated and tend to spread over the inner dural surface. These latter meningiomas represent but a small proportion of the tumours in the series, and without the microscope would hardly be recognized as belonging to the same general group. They are more common among the growths arising from the basal meninges than from the convexity, though three of them occupied the parasagittal angle and a number have been found spreading over the dura in the sphenotemporal region. In this latter situation they appear to arise from near the pterion, where the meningeal vessels and sinuses so commonly channel the bone. Though these meningiomas *en plaque* are but slightly elevated and resemble a granulomatous meningitis rather than a new growth, they are particularly prone to push through the dura and to invade the overlying bone.

This tendency of the meningiomas to provoke a cranial hyperostosis

¹ An example of one of these lesions, which are particularly apt to be associated with an overlying hyperostosis cranei, has been recently reported in another connection [9].

constitutes a story by itself, and it must suffice to say that a considerable percentage of all these tumours produce a marked effect on the adjacent bone. There may be a very slight involvement of the inner table (as in fig. 1), or a marked endostosis corresponding approximately to the centre of the area of dural attachment which is indented thereby. Occasionally the bone is enormously thickened over the growth, as much as three or four centimetres in extreme cases, and under these circumstances the canaliculi are filled more or less extensively by tumour cells, which in time may replace the thickened bone by a core of solid tumour. These characteristics are schematically shown in the accompanying

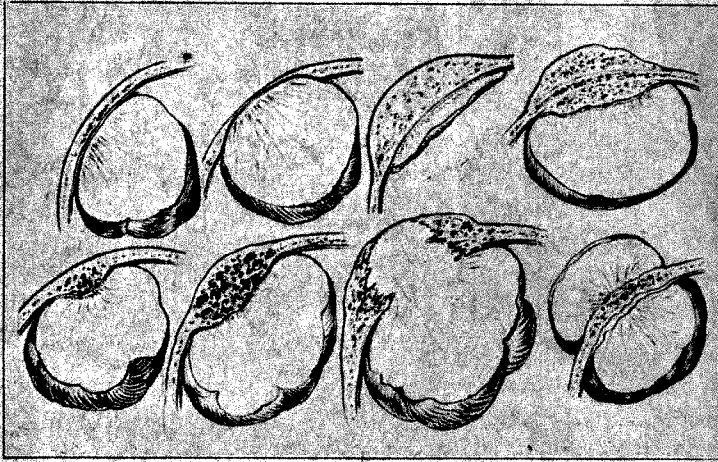


FIG. 12.—Diagrams of the various ways in which the meningiomas affect the overlying bone.

drawings (fig. 12), and they are mentioned because the photographs, X-rays and measurements giving the situation of these hyperostoses have been an additional help in placing the situation of a number of the tumours in the series. There are other ways by which the location of the seat of origin may be identified with fair accuracy, though chief reliance has been placed on the sketches and diagrams of the operations which accompany the old case records.

With due allowances, the plotted charts (figs 13 to 16) are sufficiently dependable. Though self-explanatory, there are certain features to which attention may be called. It is evident that the lesions are more numerous in the frontal regions, both of the vault and base, so that the frontal lobes have been involved through deformation far more often than any other part of the brain. Many years ago attention was

called by Blackburn [5] to the fact that frontal endotheliomas are a not infrequent post-mortem finding in those who have died in asylums, but until these diagrams were made I would not have believed that the tumours in our surgical series would, on the whole, have tended to be so far forward.

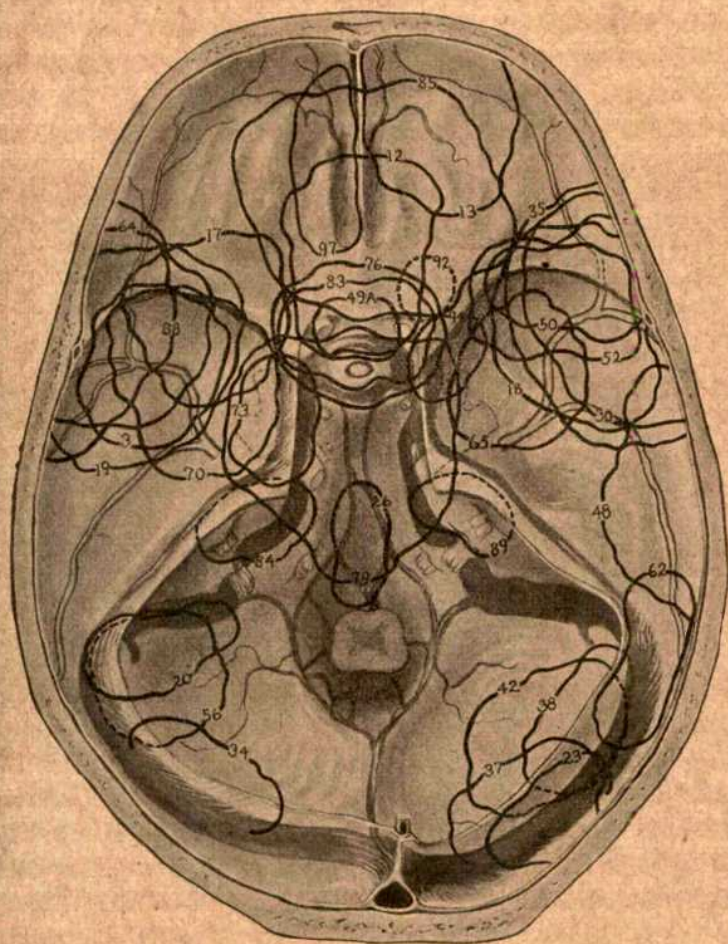


FIG. 13.—To show the areas of dural attachment of the meningiomas in the series in their relation to the major sinuses of the basal meninges.

Unquestionably many of these lesions are never recognized during life, and even if a diagnosis of "tumour suspect" actually be made, the localization of the lesion may be extremely difficult in the absence of an area of hyperostosis, either palpable or shown by X-rays. It is possible, therefore, that the blank areas in the diagrams merely repre-

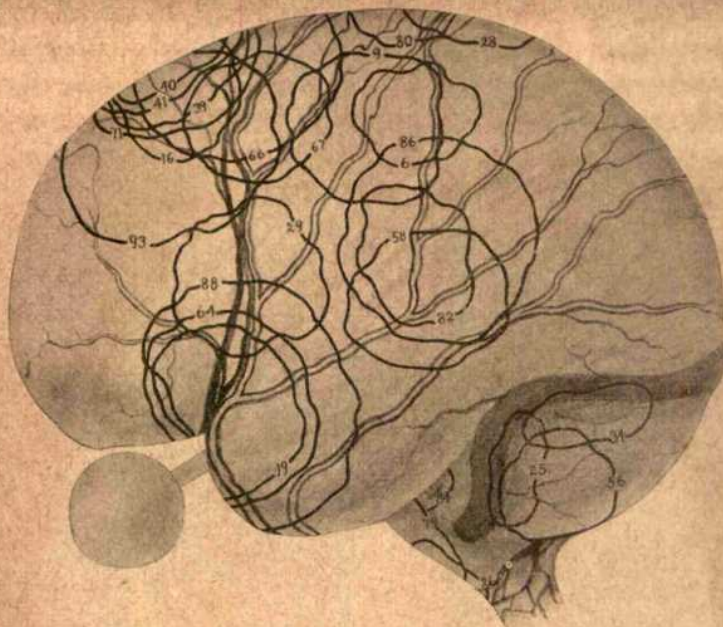


FIG. 14.—To show areas of dural attachment of the meningiomas and their relation to the dural sinuses on the left lateral aspect of the brain.

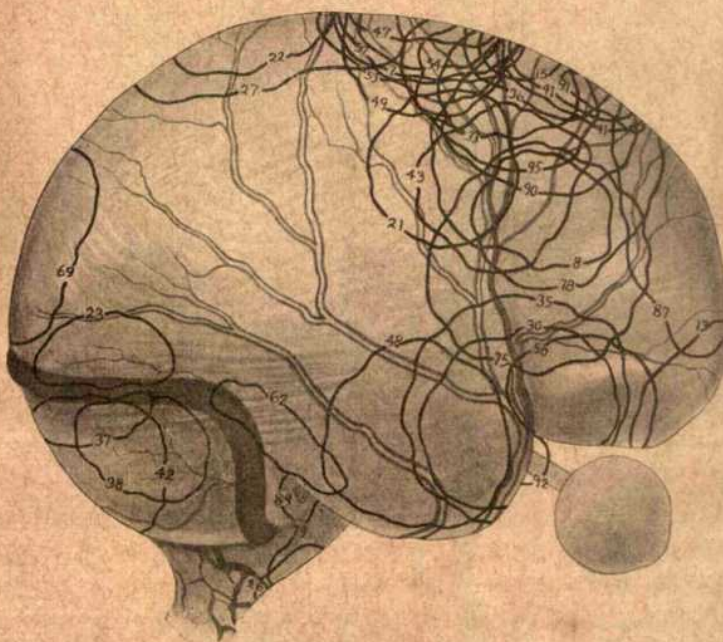


FIG. 15.—To show areas of dural attachment of the meningiomas and their relation to the dural sinuses of the right lateral aspect of the brain.

sent relatively silent fields in which tumours are less likely to have been recognized clinically. One point in favour of this is the fact that the recorded tumours show a wider distribution over the left than over the right hemisphere. The single example of tumour far posterior on the

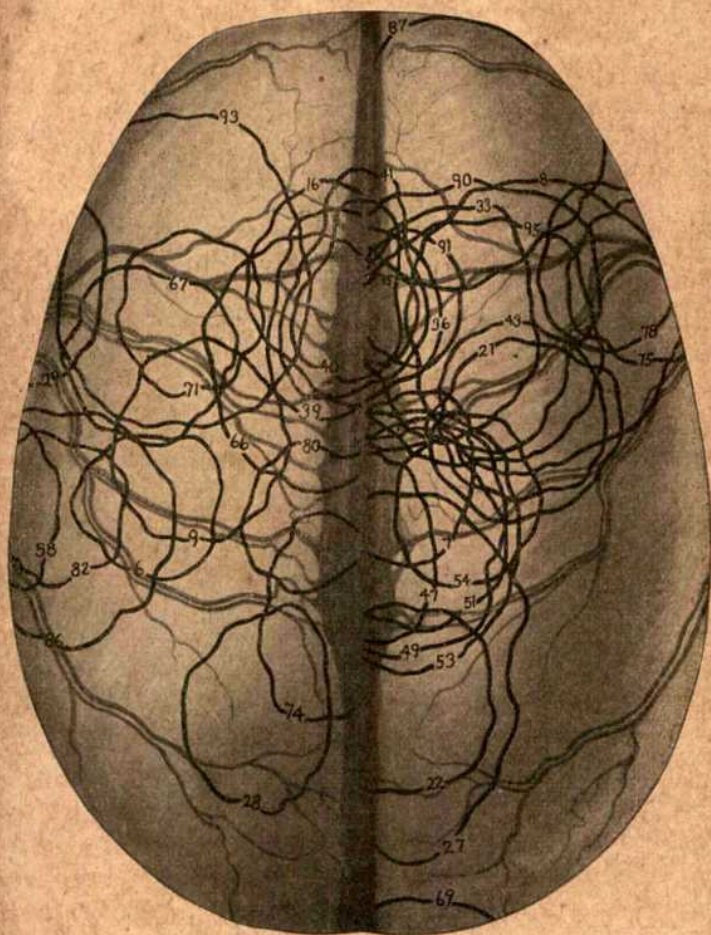


FIG. 16.—Superior view of the meninges, showing the tendency to an anterior disposition of the tumours, and the prevalence of their origin from the lateral expansion of the sinus sagittalis.

convexity of the right hemisphere (No. 27, fig. 19) was a purely accidental post-mortem finding. The patient was an acromegalic with a primary optic atrophy and homonymous hemianopsia attributed to a pituitary adenoma, and owing to the combination of his profound psychosis and an inaccurate clinical history he passed through our

hands with the meningioma unsuspected. He died a year later in an asylum, where at autopsy a large parasagittal meningioma (fig. 17) was unexpectedly disclosed.

Mere diagnostic oversight, however, cannot alone explain the predominance of anterior lesions, for notably in the posterior fossa under the tentorium, where localization should be easy, meningiomas are particularly rare. This is true, also, of the growths involving the occipital lobe, of which there have been only three in the series,

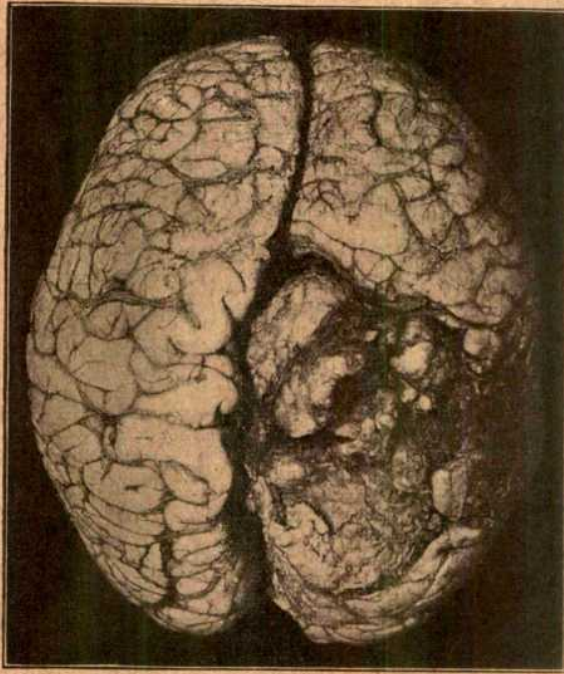


FIG. 17.

whereas on the other hand the extraordinary prevalence of tumours which take their origin from the meninges of the suprasellar region and cribriform plates of the ethmoid cannot be accounted for on the basis of chance alone.

I have spoken of the three ways of approaching the study of a large series of tumours and, so far, have refrained from any discussion of the meningiomas according to their locality. The endeavour has been made with no great success to subdivide them for working purposes into several clinical groups. These may deserve a brief mention.

(1) *The spinal meningiomas.*—These occur at different levels of the cord, and judging from my small series of twelve cases in which the greater number are midthoracic, they arise more often from upper than lower areas of the spinal theca. They are well-known lesions, frequently operated upon with success since 1888, when Horsley and Gowers so brilliantly led the way. What, however, is not commonly recognized, or at least emphasized, is the fact that they take their origin from the arachnoid at the point of emergence of one of the nerve-roots, so that the growth usually lies at the side of the cord, and is overlain by the nerve-root in question. This explains the characteristic discomforts of these cases, and the frequent tendency to a Brown-Séquard type of spinal palsy.

(2) *The cranial-nerve foraminal tumours.*—These cases fall into three groups, though they may be capable of greater subdivision since the cell-clusters from which they arise are said to exist at the foramina of exit of all the nerves. The tumours we have encountered have arisen (a) at the porus acusticus with loss of hearing as the inaugural symptom, suggesting an acoustic neurinoma (1 case); (b) from the trigeminal sheath, a common seat of origin, with trigeminal pain and hypæsthesia as early symptoms (5 cases); and (c) in the orbit itself, from the arachnoid sheath of the optic nerve, producing a unilateral painless exophthalmos (1 case).

A peculiarity of the basilar tumours, particularly those of the trigeminal region, is that they may spread widely in the basal meninges and become thereby irremovable. This, however, is not invariable, for one tumour (No 26) in the series which arose from the dura over the basilar process just within the foramen magnum, was egg-shaped with a small stalk of attachment.

(3) *The suprasellar tumours.*—These are fairly common, the series containing eight examples. The tumours arise from the meninges covering the Willisian circle of sinuses surrounding the pituitary diaphragm. Except for the fact that they occur in adults, whereas the suprasellar tumours originating from the cranio-pharyngeal pouch (Rathke) usually give symptoms in childhood, the manifestations of the tumours of the two types are very similar, consisting chiefly of primary optic atrophy, of field distortions often with hemianopsia, and finally of secondary dyspituitarism.

The growths may project upward into the region of the third ventricle, and may reach an enormous size. As several of them have been unexpectedly encountered at operations conducted for presumed pituitary tumours, they have merely been verified by the removal of a

small fragment of tissue and, except in one instance where a small, easily dislodged tumour was found, no attempt has been made to extirpate them. Consequently, except for the two cases encountered at autopsy, both of which show a remarkable similarity, the exact delimitations of the areas of attachment are somewhat conjectural.¹

(4) *Tumours arising from the olfactory groove of the ethmoid.*—In Cruveilhier's plate one of these characteristic growths is pictured, and the later literature contains reports of many others in the same situation. Though more anterior than those just referred to as suprasellar, the growths have very much the same appearance. They are exceedingly difficult to diagnose. Occasionally a fortunate stereoscopic X-ray may show some local bone absorption and unexpectedly reveal the situation of the lesion, but otherwise there may be nothing more than some obscure mental derangement possibly with anosmia until the growth extending backward reaches a sufficient size to press upon one or both optic nerves. The tumour may be median and separate the two frontal lobes widely, or, if unilateral as in the single case in the series in which a total extirpation was successfully accomplished, it may press upon the homolateral optic nerve and give a primary atrophy, whereas the opposite eye shows a choked disc.

(5) *Sphenoidal ridge tumours.*—The growths which lie astride the sphenoidal ridge, with a portion of the tumour resting on the orbital plate under the frontal lobe and a portion in the middle fossa indenting the temporal lobe, are fairly common and characteristic. Most of them have been unexpected findings, though one or two have been recognized because of an absorption of the sphenoidal ridge shown by an antero-posterior röntgenogram. They may cause uncinat seizures and not infrequently encroach on the side of the chiasma and produce an homonymous hemianopsia.

(6) *Sylvian cleft tumours (temporo-frontal).*—These are, on the whole, similar to the above and doubtless arises from the same sinus, but they lie sufficiently far lateralwards to be brought into view by a subtemporal decompression. Two of them which gave no localizing symptoms were unexpectedly disclosed in this way and were subsequently removed by an osteoplastic exposure. In this region, too, for some unexplained reason, the tumours *en plaque* are common, and as these meningiomas are apt to provoke hyperostosis and cause a palpable thickening of bone at the temporo-sphenoidal junction, they are easily

¹ One of these cases was fully recorded because of its pituitary manifestations in my monograph, "The Pituitary Body and its Disorders," 1912, Case No. viii, pp. 63-72.

recognized through this indication of their presence, as well as by the marked exophthalmos which occurs, if the hyperostosis involves the outer orbital wall.

(7) *Tumours of the convexities*.—These, twenty-eight in number, naturally represent a large proportion of any surgical series. They are not only easily accessible, but when they encroach on the sensori-motor cortex, characteristic and well-known symptoms of definitely localizing value are often produced. For this reason, small surface meningiomas which cause Jacksonian seizures followed in time by palsy not uncommonly fall to the lot of the general surgeon.

The tumours arise from arachnoid cell-clusters in connection with the sphenoparietal sinus and the vasa meningeae media. They may be subdivided into *temporal*, *frontal*, *paracentral*, *parietal* and *occipital* tumours, and the diagrams show that in spreading up from the last described group which centres around the Sylvian notch, they dispose themselves in some correspondence with the fan-shaped distribution of the sinusoidal veins of the dura. They predominate over the frontal areas and their points of origin may be found even as far forward as the tip of the lobe. The series contains no examples of tumours arising over the posterior surfaces of the hemispheres except those which take origin from the major sinuses. They are included in the following groups:—

(8) *The parasagittal meningiomas*.—These, in a way, are the most interesting and characteristic of all. The case (No. 15) selected as a text for this lecture was of this type, and the series contains twenty-six other examples. The tumours arise from the wall of the sinus or its lateral expansion, and are apt to have some attachment to the surface of the falx as well. Consequently, as the growth enlarges, the mesial edge of the hemisphere gets pushed away to a greater or less extent from the parasagittal angle.

When a parasagittal tumour is surmounted by a dome of hyperostosis, its situation and identity are easily recognized. Also when Jacksonian seizures originating in a foot are followed in the course of years by a spastic paralysis which begins in the corresponding leg, one may feel reasonably assured that a parasagittal meningioma will be disclosed at operation, provided the mesial edge of the hemisphere can be brought into view.

When, on the other hand, the parasagittal tumours arise well in front of the motor cortex or, what is less common, posterior to it, they may be exceedingly difficult to localize by symptoms alone. An example

of this has already been cited in connection with Case 27 (fig. 17). There have been only two tumours in the series deforming exclusively the occipital lobe. One of them (No. 69, figs. 15-16), a parasagittal tumour originating near the tentorial angle, was successfully enucleated with perfect recovery. The other, a huge 200-grm. tumour not represented in the diagram as its point of origin remains obscure, was incompletely removed, and there was a continuance of the growth with fatality at a secondary operation some years later.

(9) *The meningiomas of the falx.*—No mid-line diagrams permitting the representation of these tumours have been made, for the series contains only two examples. Both of them were large tumours of almost spherical form, with the smallest possible area of attachment at the lower margin of the falx. Their presence in each case was identified by exploratory punctures, and both were removed by transcortical incisions with death in one case and recovery in the other.

This I cannot believe represents fully the true percentage of tumours originating from the sides of the falx, for bony plaques and endotheliomatous patches, as is well known, are not uncommonly found there in the ordinary run of post-mortem examinations on old people.

(10) *Tumours of the sinus transversus and sigmoides.*—The series contains only two supra-tentorial tumours of this origin (Nos. 62 and 23, fig. 15). One which gave no localizing symptoms was first unexpectedly exposed during a right subtemporal decompressive operation. Its comparatively small attachment corresponded to the knee of the sigmoid sinus. One other (No. 23) was farther posterior, a large tumour which had caused a hemianopsia.

On the other hand, there have been five subtentorial tumours giving a cerebellar syndrome. All of them arose from the lower wall of the transverse sinus, and all were successfully removed at operation. I confess to some surprise that these growths are not more common in this situation, in view of the abundance of arachnoid villi which project into the subtentorial wall of this sinus and which all surgeons familiar with cerebellar explorations have been accustomed to observe.

These, then, are the chief topographical subdivisions into which the tumours have been tentatively grouped for clinical purposes. Doubtless some far better regional classification will be made as the particular symptom-complex called forth by a growth in these several regions comes to be more clearly understood. Certain of them, like the parasagittal tumours which impinge on the motor cortex, can with a fair

degree of diagnostic accuracy be foretold before operation, but in the absence of an accompanying hyperostosis most of the others are as yet chance findings in the course of an exploration, though a long history of slowly advancing trouble may make one suspect the presence of a meningioma.

I hope some day, using this lecture as a basis, to give the detailed report of the individual cases in this series with their triumphs as well as their tragedies. Our experience may be summarized as follows: (1) A few of these tumours have been accidental post-mortem findings in patients in whom brain tumour was unsuspected; (2) three of them have been late post-mortem findings in patients who had been operated upon some years before for presumed tumour, but as this procedure revealed neither tumour nor tension the cases had been variously diagnosed as some condition other than tumour; (3) in some of the cases (possibly ten) the growth, which produced no localizing symptoms, was accidentally disclosed during the course of a subtemporal decompression; (4) in the majority of the cases the presence of a tumour was obvious and its location definite, but there is no pre-operative statement in the case history to show that its nature was anticipated; (5) in a few of the operated cases not only was the location of the tumour evident, but a presumptive diagnosis was made of its character. This, of course, applies to all tumours with hyperostosis, as well as to several trigeminal, suprasellar and parasagittal lesions without osseous changes. Naturally, if one makes a diagnosis of meningioma in all patients with symptoms of brain tumour, he will be correct in about 10 per cent. of his cases, but we should aspire to something far better than this low figure

The foregoing rough subdivision is made in order to encourage others and to spur ourselves in an effort to enlarge the percentage of cases falling in the last group. Certainly, with our present knowledge of these lesions we should to-day with a corresponding group of cases be able to make a correct pre-operative diagnosis in at least half of them. Small tumours such as those described by Schmidt as accidental post-mortem findings give no recognizable symptoms and have no surgical bearing unless they happen to impinge upon some important cortical area and provoke Jacksonian seizures. But the larger tumours, even when in silent areas, ought to be capable of recognition if chronology and duration of symptoms, age of patient, extracranial circulatory signs and the frequent hyperostoses are taken into account. Accordingly, it should be possible in an ever increasing percentage of cases to foretell

not only the situation of the growth, but to anticipate its character as well. This, in an operation so elaborate as one for brain tumour, is an enormous advantage.

There is no gainsaying that despite the enucleability of these tumours when they are easily accessible the operations are often attended with great hazard, and more often than in the case of other tumours this must be done in two or even three sessions. One reason for this is that before its presence has been even suspected, the growth may have attained a large size, and by venous stasis have greatly increased the vascularity of scalp and bone.

There is to-day nothing in the whole realm of surgery more gratifying than the successful removal of a meningioma with subsequent perfect functional recovery, especially should a correct pathological diagnosis have been previously made. The difficulties are admittedly great, sometimes insurmountable, and though the disappointments still are many, another generation of neurological surgeons will unquestionably see them largely overcome.

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NOTICES OF RECENT PUBLICATIONS.

The Mechanism of the Brain and the Function of the Frontal Lobes

By Professor LEONARDO BIANCHI. Authorized translation from the Italian by James H. Macdonald. Pp. 384. Edinburgh. E. and S. Livingstone. 1922. Price 21s. net.

Professor's Bianchi's views on the functions of the frontal lobe are based on numerous experiments on the brains of animals, chiefly monkeys, carried out over a long period of time. Interpreting the results of these experiments in the light of his study of the evolution and structure of the frontal lobes and of the pathways connecting them with the rest of the brain, as well as the various doctrines of neuro-physiology to which that study gives rise, Bianchi is convinced that in man these lobes are specially concerned in the synthesis and elaboration of the higher intellectual and sentimental processes, and all the various attributes of sociality. They play a most important part, he holds, in the formation of the psychic personality, and the development of the powers of conscious volitional behaviour.

Professor Bianchi divides the cerebral cortex into two main evolutionary levels, the postfrontal motor and sensory areas, and a prefrontal area that is neither motor nor sensory; he also postulates two grades of psychic activity, a "lower" and a "higher" consciousness, resulting from the activity of these two levels. In the lower or postfrontal consciousness, only the simplest mental constructions obtain; life is centred around sensations, desires, and instincts; conduct is impulsive and egoistic, and tends to the immediate satisfaction of individual needs only. In the higher or prefrontal consciousness, reason and all the potentialities of thought come into play; and impulses become subject to voluntary inhibition and control and are influenced by factors arising from the development of the more lofty sentiments and the higher social tendencies and obligations. When Bianchi speaks of the higher consciousness as prefrontal he does so only in the sense that it is the prefrontal area of the cortex that contributes to it its most weighty factors. Its centre of centres is in the prefrontal area, but it is necessarily open, he maintains, to currents from all parts of the cerebral mantle, and it thus comes to form with the lower consciousness a wide network of ideas and experiences which embrace the products of all the cortical centres. That power of starting, directing, evoking and selecting the nervous currents, possessed in a minor degree by all the cell-groups of the cortex, belongs in supreme part to the prefrontal area. In Bianchi's view, therefore, the frontal lobes are the seat of the final synthesis and fusion

of the incoming and outgoing products of the several sensory and motor areas of the brain.

The work of the brain, as a whole, is carried on by processes occurring in different levels of physiological complexity, the later and more highly evolved areas assimilating, synthesizing, and modifying the products of other lower subsidiary levels, and in dealing with the highly complex psychical end-products of prefrontal synthesis. Bianchi sees no reason for treating them differently from the other products of cerebral activity of a more physical character, or thinking that their governance is by laws in any essential way different from those that obtain in the more purely physiological sphere. He discusses the results of frontal lobe activity, therefore, wholly as biological products, not as spiritualistic or metaphysical abstractions, and in doing so necessarily lays the greatest stress on the multitudinous combinations of innumerable lesser grade compounds in their final elaboration. What it involved in the last analysis, in the psychic transmutation or "mentalization" of matter, may be still open to conjecture, but even here Bianchi offers some suggestive speculations in regard to the light which the study of the behaviour of electrons may throw on the subject.

Professor Bianchi's opinions concerning the function and relationship of the different parts of the brain, founded as they are on the results of extensive experimental investigations, must command our respect, while his careful attempt to evaluate psychic phenomena on a biological basis affords us no slight glimpse into the mechanism of the brain's activity, and serves as a stimulating corrective to those aspects of psychological thought which tend to divorce mental processes from their physical substratum. His insistence too, at the end of his book, on the primary importance of rightly trained, conscious intention and intelligence in the conduct of the practical affairs of life is especially valuable at a time when, too often, the "urge" of the unconscious is apt to be used as an excuse for the lack of that self-control and sense of responsibility, for the cultivation of which he pleads. He expresses "grave doubts" indeed, of the automatism of the unconscious, apart from any directive effect due to the action of the conscious will.

A word in conclusion must be said about the translation of this book. Dr. Macdonald has done this in a way that cannot be too highly praised, and has given us a scholarly English version, in all respects worthy of its distinguished author.

Questions neurologiques d'actualité. Pp. 551. Paris: Masson et Cie. 1922. Price 28 francs.

In this volume there are collected together twenty lectures on neurological subjects of special interest delivered before the Faculté de Médecine de Paris in 1921. Each of the lecturers was free to choose the subject that appeared to him of most importance at the moment, and each subject selected has been consequently dealt with by one capable of placing before his audience views of an authoritative and reliable nature.

In most cases the aim of the lecturer has evidently been to put forward the observations and opinions on his subject that appeared at the moment most trustworthy rather than his own personal views, but many of the articles show evidence of original investigation and research. In some instances, however, the lectures are based on the original investigations of the authors, this is particularly so in Kinnier Wilson's contribution on the pathogenesis and pathological physiology of progressive lenticular degeneration, and in Pierre Marie's discussion of the question whether preformed and innate centres for speech exist in man. In both of these, as well as in Claude's paper on intracranial hypertension and serous meningitis and in Lhermitte's on lethargic encephalitis, in which the subject matter consists mainly of original work already published, we are fortunately provided with the views these neurologists hold to-day after reviewing their earlier work in the light of further experience and criticism. A few of the lectures on the other hand merely represent the ordinary teaching of the day, without any analysis or critical selection of facts and hypotheses.

There are, however, few of these lectures which will not repay perusal by any neurologist, and all will be valuable to the general physician and even to those specialists who are unable to keep pace with the neurological literature.

The only serious fault that can be found with the volume is absence in almost all the articles of bibliographic references to the work of others which is cited.

Report of the War Office Committee of Enquiry into "Shell Shock."

H.M. Stationery Office. 1922. Price 6s.

The reference to the Committee was to collate the expert knowledge derived by the Naval and Military Authorities and the medical profession from the experience of the war with a view to recording for future use the ascertained facts as to the origin, nature and remedial treatment of "shell shock," and as to whether by military training or education some scientific method of guarding against its occurrence could not be devised.

In a brief note on this report, it is scarcely necessary to enter into a consideration of the more purely military aspect of this subject, but a summary of the medical findings may not be without interest.

It was agreed that "shell shock" had been a gross and costly misnomer, and that the term should be eliminated from the nomenclature. The war produced no new nervous disorders, all those which occurred had previously been recognized in civilian practice. Owing to the special circumstances of the war these disorders appeared in some cases in an aggravated form, and the numbers suffering from them were very large.

The cases divided themselves into three main groups: genuine concussion without visible wound; emotional shock, either acute or developing slowly as a result of prolonged strain and terrifying experience, the final breakdown being

sometimes brought about by some relatively trivial cause; and nervous and mental exhaustion the result of prolonged strain and hardship. In many cases, however, the three factors of commotional and emotional shock and exhaustion were combined in varying proportions.

Many points of interest have been brought to light and the verbatim evidence of witnesses is by no means the least instructive part of the report. Here will be observed personal experiences bearing upon the psychology of fear, upon cowardice, upon malingering, upon the influence of war stress in the production of insanity, and valuable recommendations upon the prevention of "shell shock."

The treatment of the neuroses observed in soldiers is considered in detail, and the several forms of psychotherapy are commented upon with fairness and discretion.

The report may have a much wider significance than was intended when the idea of an inquiry was broached, as it deals with psychological problems which are not confined to war conditions.

Remembering and Forgetting. By T. H. PEAR. Methuen. Price 7s. 6d.

The analysis of dreams has been described as the royal road to the understanding of the unconscious. If we broaden the issue by substituting memory for dreams we will find that it becomes the nuclear problem of modern psychology, the full appreciation of which can only be obtained by the analysis of Memory and Forgetting.

This is the task that Professor Pear has undertaken in his book, designed primarily for the interested layman and the medical man who is interested in the psychological problems of medicine.

Being engaged in the elucidation of the experimental and theoretical problems of normal psychology, Professor Pear has not approached the subject in the manner of the psycho-analyst—that, is by plunging directly into the concrete details of the mental life—but begins by an analysis of memory processes from their genesis at the perceptive level, to the formation of after-sensations; thence to visual, auditory and kinæsthetic imagery, and ultimately to the formation of generic images upon which our ideas are based. This prepares the way for a consideration of the dream-life. The Freudian conception is fully considered, as well as the additions to it made by Rivers. He ends his analysis by a chapter on forgetting, which in the light of modern theory is the justification of all the preceding chapters.

There are one or two features of the author's method which make his treatment of the subject somewhat insufficient. Firstly, his own annoying visual imagery makes the subject appear easier than it actually is, although he does not fail to emphasize the importance of kinæsthetic imagery; and secondly the insufficient stress laid in the earlier chapters on dreams on the affective tone of the memories in dreams.

The two essays on synæsthesia and number forms are important for the psychology of imagery, and have an indirect bearing on the subject of remembering.

The whole book would well repay reading even to those engaged in applied psychology, for it deals with the theoretical basis of memory. It is written in a clear and succinct style.

Suggestion and Mental Analysis. By WILLIAM BROWN. Pp. 165.
University of London Press. 1922. Price 3s. 6d.

The author is of the opinion that the two main forms of psychotherapy, that is suggestion and mental analysis, are not mutually exclusive as the extreme partisans of each system maintain. The aim of this small book is to give an elementary and non-technical account of their relations to one another, and to show that by harmonizing them as far as possible a sound system of psychotherapy can be built up.

The earlier chapters form a concise and in the main a sufficient introduction to the subject for the layman and non-specialist for whom the book is written, while the last three deal chiefly with Bergson's philosophy and the relation it bears to the author's own views.

Though written in a simple and clear style the book lacks the cohesion so necessary in an elementary text-book.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

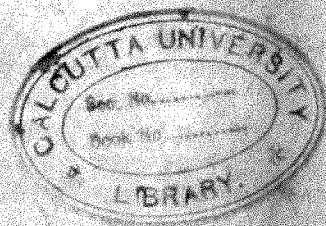
To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

[DECEMBER, 1922.]

BRAIN.

PARTS 3 and 4, VOL. 45.



TWO CASES OF SYRINGOMYELIA AND SYRINGOBULBIA, OBSERVED CLINICALLY OVER MANY YEARS, AND EXAMINED PATHOLOGICALLY.

BY JAMES TAYLOR, M.D., F.R.C.P.

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Pathologist,

AND

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Senior House Physician to the Hospital.

SYRINGOMYELIA, although perhaps not so unusual as at one time it was supposed to be, is a very interesting disease, because of the clear association which it is possible to trace between the anatomical change in the spinal cord and bulb, and the clinical condition. The two cases which we are about to relate are perhaps unusual because of the long periods during which it was possible to observe them carefully. They also have a special interest because of the striking manner in which the clinical course differed in the two cases. In the first patient the condition underwent no change of consequence during the long period of twenty-four years in which one of us (J. T.) had him under almost continuous observation; in the second, who was also under observation for a long period, viz., nineteen years, there was on the contrary a slow but steady deterioration in the physical condition determined by the gradual spread of muscular weakness and sensory change, the result no doubt of corresponding changes in the condition of the spinal cord. The detailed description of the morbid changes in the spinal cords, for which two of us (J. G. G. and J. P. M.) are responsible, explains to some extent this difference.

H. M., a pastrycook by occupation, was admitted to the National Hospital, Queen Square, under Dr. Hughlings Jackson on May 15, 1893. He was at this time 23 years of age and had previously been under Dr. Jackson's care at the London Hospital. He said that four and a half years before admission he had experienced pain in the right occipital region, with numbness in the arms. Three months later there developed squinting of the right eye and diplopia, and a few days later there was numbness of the right side of the face and complete loss of sensation here which lasted for a fortnight. This, he said, had since practically cleared up. Four days after experiencing numbness of the face he noticed that the right side of the face was motionless, and he stated his articulation was indistinct and the tongue on protrusion went to the right. For the last four months before admission the occipital pain had been worse, and there was tingling and loss of feeling down the right arm and leg.



FIG. 1.—Case I. Patient in 1893.



FIG. 2.—Case I. Patient in 1915.

There was nothing of significance in his family history or in his personal history. He had had no serious illness and he denied venereal disease.

On admission he was found to have a marked right internal strabismus due to complete paralysis of the right sixth nerve. There was also complete facial paralysis on the same side and the tongue protruded to the right. The right side of the tongue was much wasted, and although the temporal and masseter muscles on both sides were strong and active, the jaw dropped to the left when the mouth was widely opened. There was a good deal of wasting about the shoulders, more marked on the right side, and although the trapezius and other

muscles of the shoulder-girdle all responded to a faradic current on this side, a stronger current had to be used than was sufficient to produce a good contraction on the other side. There was no wasting of the lower limbs; the knee jerks were present and there was no ankle clonus.

The sensory changes were very distinct and interesting. They are so graphically represented in the accompanying diagrams that no further description seems called for. (Figs. 3A, B and C.)

The diagnosis in this case was not difficult, and although at that time—1893—we were not very familiar with syringomyelia, there was no hesitation in concluding that this was a case of that nature. It was apparent that the morbid process had affected not only the spinal cord, especially in its cervical portion, but had also spread upwards so as to involve bulbar and pontine

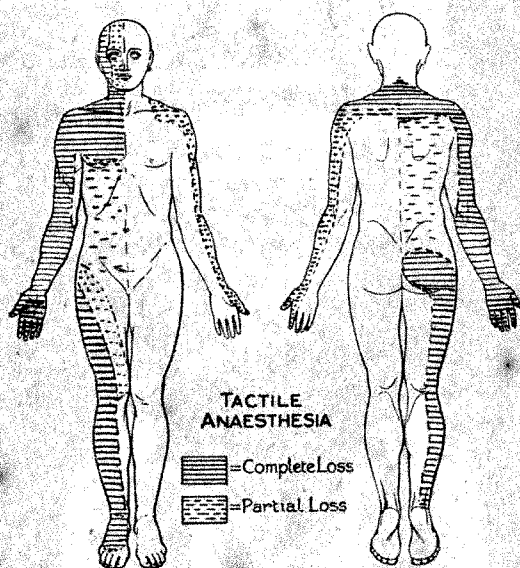


FIG. 3c.—Case I.* Tactile anaesthesia in 1893.

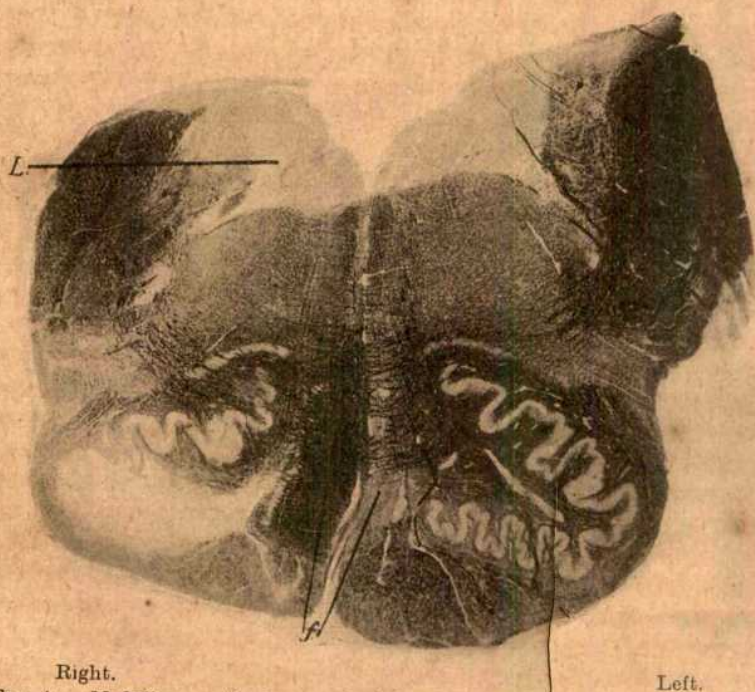
structures, as was shown in the wasting of the tongue, the facial paralysis, and the paralysis of the sixth nerve on the right side. The sensory changes also indicated involvement of the fifth nerve or its nucleus.

The patient during the next twenty-four years was seen from time to time and examined carefully, but no material change developed. He enjoyed fair health, although he complained a good deal from time to time of pains in his head and limbs. He married but had the misfortune to lose his wife in 1916 and became very much depressed. He committed suicide by hanging in the following year, having previously asked his brother-in-law to communicate with one of us (J. T.) if anything happened to him. Through the kindness of the Coroner a post-mortem examination was allowed, but as this was not carried

out until forty-eight hours after death the sections of the cord were not as good as they might have been had it been possible to make the examination earlier. It will be seen that the examination confirmed the diagnosis.

CASE I.—PATHOLOGICAL EXAMINATION.

The brain and cord were fixed directly in Müller's fluid, where they remained for over a year. In consequence of this, permanent flexures had taken place at some segments of the cord and the tissue was rather brittle, so that it was impossible to avoid some distortion of the sections. The chief characteristics of the cord at each level could, however, be made out fairly well.



Right. Left.
FIG. 4A.—Medulla near the lower end of the fourth ventricle. *f.*, Mesial fillet;
L., lateral extension of the cavity.

The process of gliosis and cavitation extended from the lower half of the medulla to the lower half of the dorsal region of the cord. For the most part the cavity occupied only a small area of the centre of the cord, but was surrounded by a relatively wide zone of gliosis, in which myelinated fibres were absent.

No abnormality was found at a higher level than the upper part of the pons, but the iter of Sylvius was T-shaped, with a ventral and two lateral prolongations. The ventral one extended between the oculo-motor nuclei, but did

not reach as far as the posterior (median) longitudinal bundle. The lateral extensions almost reached the mesencephalic roots of the trigeminal nerves; they were curved slightly forwards, and their walls, which were everywhere covered with ependyma, were crenated and irregular, the ventral wall showing several small bays and creeks.

Beyond this nothing abnormal was found in the pons and mid-brain, except degeneration of ascending tracts, such as the mesial fillet on the left side, which had been interrupted by the morbid process lower down.

The highest section which showed any evidence of abnormal gliosis was one near the lower end of the calamus scriptorius, passing through the middle of the olivary body (fig. 4A). Here the fourth ventricle had a somewhat irregular contour, extending forward as a narrow slit between the hypoglossal nuclei as far as the dorsal margin of the posterior (median) longitudinal bundles. It also sent a shallower extension in on the right side between the hypoglossal nucleus and the dorsal nucleus of the vagus. Both these slits were lined with the normal ependyma of the ventricle. That in the middle line caused no distortion of fibres, but curving round the gliosis which covered the lateral slit a leash of myelinated fibres could be seen to which there was nothing corresponding on the left side.

At this level and extending downwards through the medulla for a short distance, there was a gross atrophy of the cells in the ventral portion of the right inferior olive, and, associated with this, a loss of the olivo-cerebellar fibres arising in them. An examination of sections at the highest level at which this lesion existed disclosed a small Y-shaped cavity. Its longest limb lay between the pyramidal tract and the olive; one of the shorter limbs passed ventrally and mesially through the pyramidal tract, and the other dorsally between the olive and the mesial fillet (fig. 4B). From the walls of this cavity gliosis extended into the neighbouring tissues, chiefly along the hilus of the olive for about two-thirds of its extent, but also as continuations of the limbs of the cavity. In the more caudal sections through the olive no cavity could be seen, but the presence of gliosis was shown by the increase in the number and size of the glial cells, and to it the atrophy of the ventral part of the right olive appeared to be due. The lateral part of the pyramidal tract was smaller on the right side than on the left; the shrinkage of this tract was also probably due to its involvement in the gliosis.

Unfortunately serial sections were not made through the upper part of the medulla and the lower part of the pons, part of the tissue having become unusable owing to its long stay in Müller's fluid during the war, so that it was impossible to trace the extent of this cavity; but if either the cavity itself or a band of gliosis spreading out from it, had passed upwards for a short distance in the same relative position it would have interrupted the emerging fibres of the sixth nerve.

The most obvious loss of fibre tracts was in the mesial fillet on the left side, that is, in the more normal half of the medulla. This fillet had almost completely disappeared, and the place normally occupied by it had shrunk so that



Left.

FIG. 5.—Medulla at the level of the tip of the calamus scriptorius solitarius; *f.*, mesial fillets; *L.*, lateral gliosis.

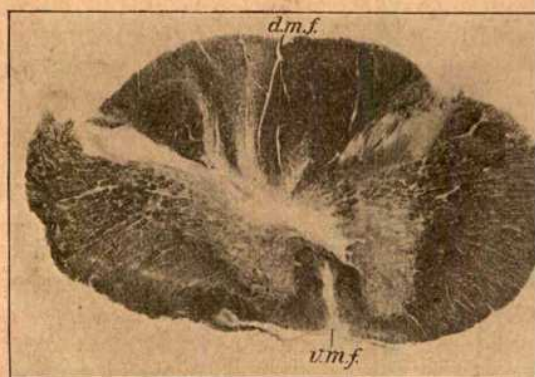


FIG. 6.—Cord at first cervical segment. *d.m.f.*, Dorsal median fissure; *v.m.f.*, ventral median fissure.

interrupted by the gliosis and cavitation which lay between the fillet and the olive, and that their cells of origin had consequently undergone a retrograde degeneration.

Spinal Cord.—In the uppermost cervical sections (fig. 6), the central canal was represented by a solid cluster of ependymal cells. Areas of gliosis were present on the left side of it and behind it in the ventral part of the dorso-median septum. From the latter area a cavity extended along the dorso-mesial aspect of the right dorsal horn, the nerve cells in which were much less numerous than on the left side. From the ventro-mesial end of this cavity an area of gliosis ran a short way into the ventral part of the column of Burdach.

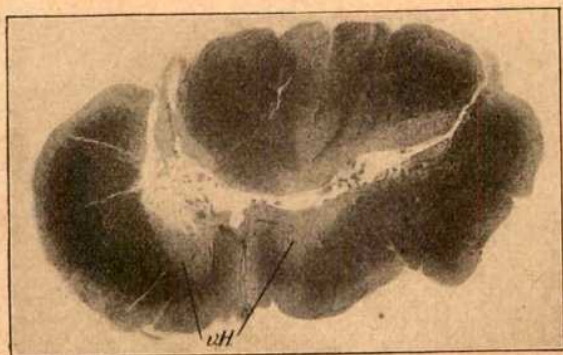


FIG. 7.—Third cervical segment of cord. *v.H.*, ventral horns.

At a rather lower level (fig. 7), the cavitation had extended through both dorsal horns and the grey commissure, occupying the situation of the central canal, of which no trace could be seen. At this level the walls of the cavity were lined with a definite layer of gliosis, which varied in thickness and, as in the higher sections, spread into the ventral parts of the column of Goll and the right column of Burdach. At the level of the seventh cervical segment the cavity had spread forward to reach the ventral median fissure, and laterally to the bases of both ventral horns. Extensions ran backwards a short distance down the left dorsal horn, and down the outside of the right dorsal horn almost to the margin of the cord. The wedges of gliosis which were seen at higher levels extending between the columns of Goll and into the right column of Burdach were still evident at this level, the lateral wedge being rather larger than it was above. Except for these wedges, the glial lining surrounded the cavity fairly regularly, and had a sharply marked outer border. The cavity itself was lined over a considerable part of its walls by a definite layer of fibrous tissue, which was continuous with the pia mater of the ventral median fissure. Many thick-walled blood-vessels lay, apparently free, within the cavity; the lumen of some of these was completely occluded, but in others red blood corpuscles could be seen.

TWO CASES OF SYRINGOMYELIA AND SYRINGOBULBIA

The gliosis round the central cavity was, however, still more marked at the level of C 8 (fig. 8). Here it assumed a modified trefoil appearance and corresponded closely to the shape and extent of the central canal of the lumbar cord in Case II (fig. 22). It extended from the ventral median fissure laterally to the bases of both ventral horns, and dorsally a short distance from the dorsal median septum; the lateral areas of gliosis were club-shaped, their outer ends swollen and rounded. Its outer border, that is the border at which myelinated fibres appeared, was everywhere clear cut and regular.

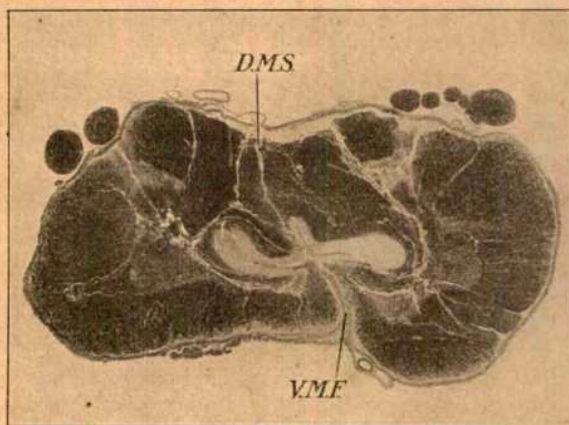


FIG. 8.—Cord at 8th cervical segment. *D.M.S.*, Dorsal median septum; *V.M.F.*, ventral median fissure.

Throughout the cervical region of the cord the nerve roots, both ventral and dorsal, were well myelinated and appeared to be of normal thickness. There was no gross atrophy of tracts apart from the areas of gliosis already described, but the left ventro-lateral column stained rather less deeply than the right.

In the upper thoracic region of the cord the gliosis was limited to an elongated oval running from the neighbourhood of the ventral median fissure through the region of the central canal and dorsally for about two-thirds the length of the dorsal median septum. In the more caudal segments this area was separated from the ventral median fissure by some myelinated fibres of the white commissure, but its shape and extent remained essentially constant. Its outer border was as definite and clear cut as in the cervical segments. The cavity, which was limited to a small slit in the centre, showed no lining of connective tissue. The white matter of the cord appeared normal at this region, except for the extreme thinness of the white commissure, and for an area of pallor extending backwards from the end of the central gliosis along the dorsal median septum. In the thoracic region this central gliosis lay definitely behind the column of ependymal cells representing the central canal of the cord, and was separated from it by a thin layer of white matter.

ORIGINAL ARTICLES AND CLINICAL CASES

It by a few fine myelinated fibres, some of which ran longitudinally, while others passed across from one side of the cord to the other.

It is impossible from the material at our disposal to determine the level of the lower end of the gliosis in the cord, but it had ceased at the level of the lumbar segment. From here downwards through the lumbo-sacral plexus and conus medullaris the central canal was represented by a fairly rounded clump of ependymal cells, which however did not show the cellular arrangement seen in Case II. Their appearance was indeed similar to that usually found in adult cords at this level.

RELATIONSHIP OF CLINICAL SIGNS TO PATHOLOGICAL CHANGES.

In this case there are several clinical signs which it is very difficult to explain by the pathological changes discovered, although others admit of a simple explanation.

The anaesthesia over the area supplied by the right trigeminal nerve was accounted for by the involvement of the substantia gelatinosa Rolandi, the degeneration in the descending trigeminal root on that side.

The wasting of the right half of the tongue was obviously a result of atrophy of the nucleus and fibres of the right hypoglossal nerve. In this and the paralysis of the right abducens nerve were probably due to the area of cavitation and gliosis which lay between the inner end of the right olive and the pyramidal tract. From the material at our disposal we are unable to give an anatomical explanation of the weakness of the muscles supplied by the fifth and seventh nerves on the right. The nystagmus may be attributed to the lesion of the descending part of the right vestibular nerve.

This case presented the unusual feature that the anaesthesia on the left half of the body was nowhere dissociated. The area of complete loss of appreciation of light touch was exactly the same as that in which pin-prick and heat and cold were not recognized, and where one form of cutaneous sensibility was reduced but not abolished, the others were similarly diminished. The apparent anomaly admits, however, of a simple explanation. It is generally believed that tactile impressions are conveyed to the thalamus by two sets of fibres; one set crosses in the cord along with the fibres conveying thermal and painful sensations to the opposite ventro-lateral column, while the other ascends in the dorsal columns to the dorsal nuclei of the medulla, and thence by spinal arcuate fibres and the mesial fillet. But in this case the fibres arising from the right dorsal nuclei to the left fillet were interrupted by gliosis which spread out from the floor of the fourth ventricle, and

menced five years before, and was first noticed after she had had an abscess over the left first dorsal interosseous muscle. This abscess was opened without an anæsthetic, and the surgeon complimented her on her "pluck." But as she laughingly observed, she deserved no credit, for the operation was absolutely painless! After this she began to have "pins and needles" in her left hand, which gradually spread up to her shoulder. Numbness was superadded, and in 1901 muscular weakness and contraction of the hand developed. She was admitted to the hospital in 1902. Apart from the weakness of the arm and hand and the anæsthesia shown in the charts (figs. 9 A, B, and C) nothing was noted except marked nystagmoid jerking of the eyeballs. She remained in hospital for two months, and was afterwards for a time at the convalescent home. There was no difficulty, even in the out-patient room, in making a diagnosis of syringomyelia, and examination in hospital confirmed the out-patient diagnosis. There was nothing significant in her personal history or family history, except that a sister had died of probably disseminated sclerosis.

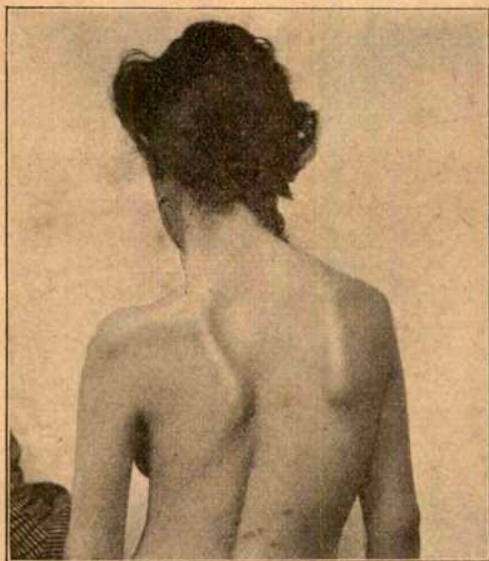


FIG. 10.—Case II. Showing scoliosis in 1905.

She was re-admitted to the hospital in 1905 and then she complained weakness of the left leg as well as of the left arm. There was no wasting of the leg muscles, but there was an exaggerated knee-jerk on this side and ankle-clonus. A definite lateral curvature of the spine had now developed (fig. 10). The left hand was a characteristic *main en griffe*, but the wasting was masked to a great extent by what has been described as a "succulent appearance of the back of the hand and fingers (figs. 11 and 12); there was

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sh redness and an appearance as if the hand were cold, although to the it felt quite warm. The wasting had spread up the left arm to affect the es of the shoulder-girdle, and there was also some wasting of the muscles right shoulder. The nystagmus was more marked than before, but the y condition was little changed.



FIG. 11.—Case II. Patient in 1905.



FIG. 12.—Case II. Showing swollen appearance of the left hand.

e was again admitted on May 15, 1909. The weakness in the left arm g had increased and there was wasting in the left calf. The plantar was now extensor on both sides, and she complained of numbness of the of the left side. There was some unsteadiness in standing and a little lty in passing urine. The trophic change in the left hand was now

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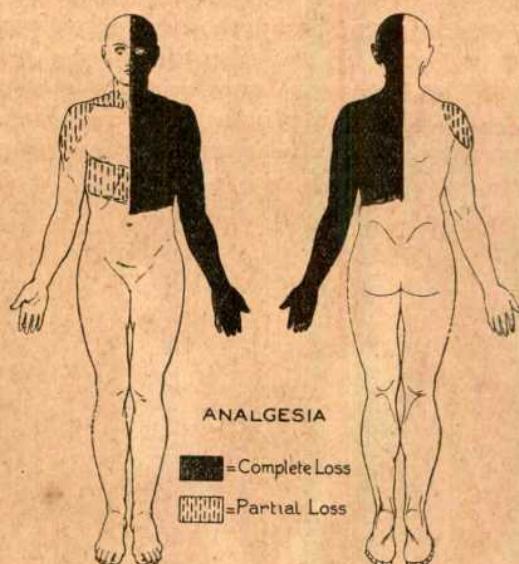


FIG. 13A.—Case II. Analgesia in 1909.

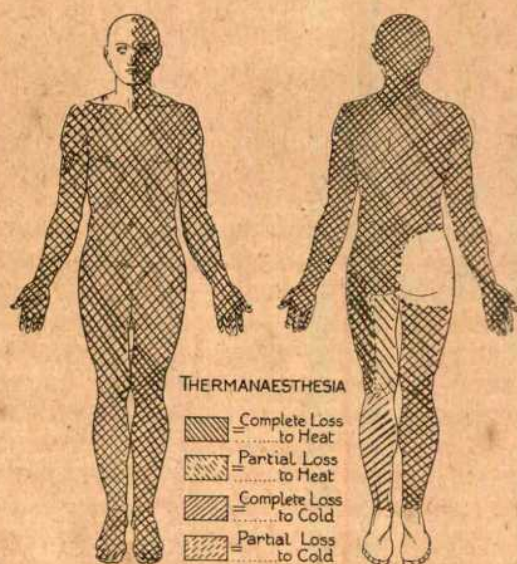


FIG. 13B.—Thermanæsthesia in 1909

more marked; the hand was swollen and of a purplish red colour all over. The sensory changes are shown in the diagram (figs. 13 A and B). She was again admitted on February 22, 1911. There was no marked change except that there was now slight wasting of the right hand, partial ptosis of the left eyelid, more marked nystagmus, and greater weakness of the lower extremities with increased spasticity of them. She had on this occasion a discharging painless boil on the right buttock; she also complained of some difficulty in articulating, although this was not noticeable. The analgesia recorded on this occasion is shown in fig. 14.

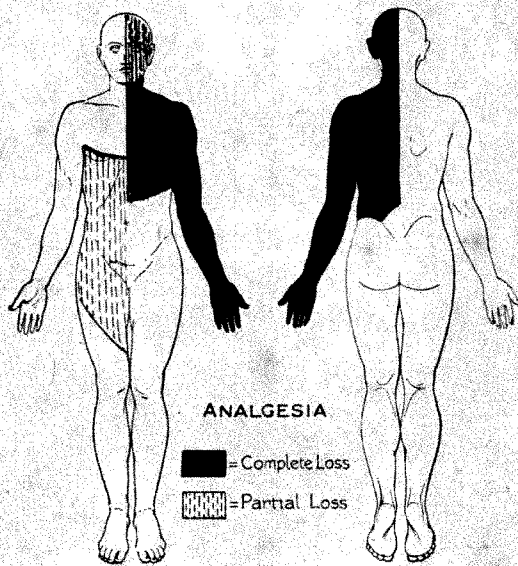


FIG. 14.—Case II. Analgesia in 1911.

She was in hospital also in 1916 but no change of consequence seems to have been noted. Her weakness in the upper limbs had increased and there was greater difficulty in walking. She was more pale and anæmic than before. There was no marked alteration in the condition of sensation.

On admission again, on March 3, 1919, her condition was one of great helplessness. She was quite unable to get about on account of the great weakness of the lower limbs, which she could only move a little in bed. Her left arm was powerless and her right almost as weak. She could not raise her head from the pillow. The nystagmus was marked and very coarse, and she complained that objects always seemed to be dancing up and down. The wasting was general but more marked on the left side; it included the sternomastoids and erectores spinæ. The knee-jerks and ankle-jerks were still active; there was bilateral ankle-clonus and each plantar reflex was extensor. The abdominal reflexes were absent, and there was some difficulty in passing

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The sensory changes then present are represented in figs. 15 A and B. She was sent to the Convalescent Home at Finchley, where she died on 13, 1921.

We have here, then, a case of a girl with nothing significant in her personal history, and the only point to note in the family was the possibility of disseminated sclerosis in a sister. At the age of 17 she had a pimple abscess on the left hand, the evacuation of which by incision was unattended by pain. The subjective sensation of numbness in the hand which was experienced a year later, in the course of four or five years spread up the left arm to the shoulder. At the age of 22, i.e., five years after the first symptoms appeared, she came under observation with wasting of the left arm and the disturbance of sensation depicted in the text. From this time onwards there was a slow but steady extension of numbness, wasting and weakness, with signs indicating involvement of the lateral columns and of the fifth cranial nerves. The muscular wasting and consequent weakness resulted in almost complete immobility of the limbs and trunk, and the sensory impairment also extended. Death occurred at the age of 42, twenty-five years after the commencement of the illness.

PATHOLOGICAL EXAMINATION.

A post-mortem examination was made on April 14, 1921.

The body was generally emaciated, but there was especially severe wasting of both upper limbs, perhaps rather greater on the right side than the left. There was a recent acute bed-sore over the back of the right shoulder.

The brain and cord were removed and suspended in 10 per cent. formalin solution.

The brain was abnormally long, measuring 19 cm. in length and 14 cm. in breadth. There was a slight degree of hydrocephalus, the anterior and posterior horns of the ventricles being about 2 cm. wide and having rounded tips. Apart from this the brain showed no gross abnormality above the level of the cerebellum.

The cord in the lower cervical and upper thoracic regions was a very thin, thread-like tube, filling the spinal canal and containing clear fluid like cerebrospinal fluid.

After fixation in formalin pieces from each of the segments of the cord were placed in Weigert's primary mordant, the cavity in them being filled with threads of pyroxylin. These dissolved out during the further processes of embedding in celloidin, leaving rings of spinal cord in much the shape that they would have assumed during life. Transverse sections from the mid-brain, pons, and medulla (the lower part of which was cut in serial sections), and from each of the spinal segments, were stained both by the Kultschitsky-Pal method, and by alum-haematoxylin with van Gieson's counterstain.

Pieces of the left ulnar nerve and a branch of the median (probably a sensory branch), and of the flexor sublimis digitorum and flexor carpi ulnaris

only was all the area behind it more or less degenerated, but it would appear from comparison with the right side that there had been considerable loss of tissue. The most dorsal part of the twelfth nucleus, the dorsal bundle of Schütz and the dorsal nucleus of the tenth and eleventh nerves, having lain in the line of the slit, were missing, and the descending nucleus of the trigeminus could not be distinguished. Dorsal to the slit the nuclei of the posterior columns were destroyed by gliosis, and the fasciculus solitarius showed degeneration and was devoid of surrounding cells. The area of the pyramidal tract was pale on both sides, especially on the right, some of its fibres having degenerated up to this level (retrograde degeneration). Emerging fibres of the hypoglossal nerve were fewer on the left than on the right, and though the nucleus of the nerve showed no gliosis it was deficient in cells.

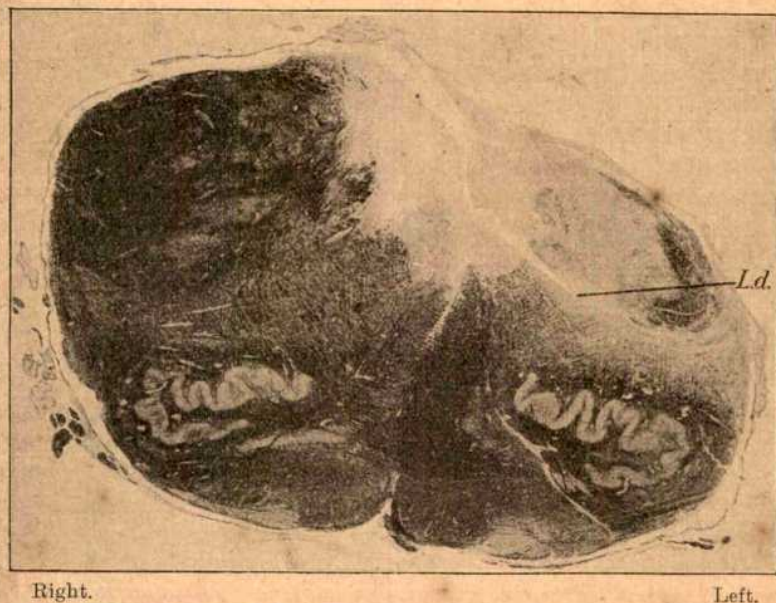
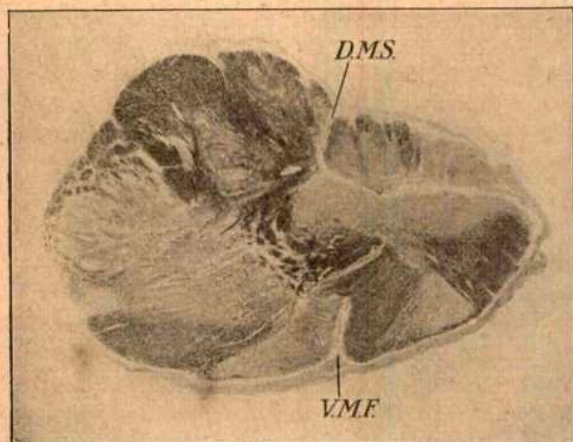


FIG. 16.—The right mesial fillet is severely degenerated, and the left fasciculus solitarius has almost disappeared. *L.d.*, Lateral diverticulum or slit.

In the lowest part of the medulla (fig. 17) the amount of gliosed tissue was much smaller relative to the cavity than at the level of the calamus, and at the decussation of the pyramids the loss of tissue on the left side of the medulla had been so great that this side was only about one-third the size of its fellow. The slit had inclined ventrally on attaining this level and had reached the periphery on the left, while in front of it a column of gliosis had formed round the central canal. By the erosion on the left side the left pyramidal tract had been completely destroyed just after it crossed, and by



Right.

Left

FIG. 17.—The whole of the right pyramid and the lateral part of the left are degenerated. The internal arcuate fibres coming from the right dorsal column nuclei stain normally, but those from the left have disappeared. *D.M.S.*, dorsal median septum, *V.M.F.*, ventral median fissure.

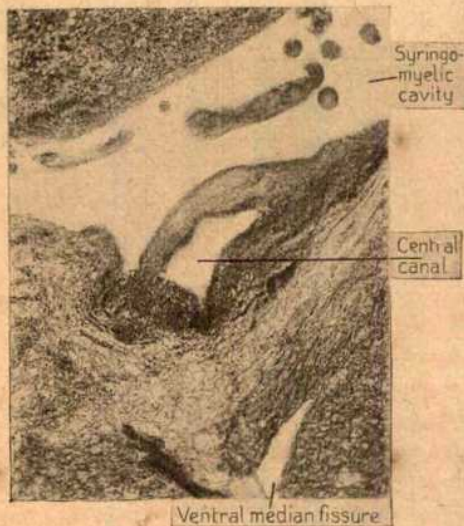


FIG. 18.—Case II. Cord at level of second cervical segment.

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gliosis round the central canal those fibres of the right pyramidal tract which had lain most posteriorly in the decussation were also interrupted. The ruptured fibres on both sides evidently degenerated both upwards and downwards from the lesion, with the result that immediately above its decussation the right pyramid was almost entirely degenerated and the left pyramid at the same level showed degeneration of its lateral part; the descending degeneration had an important influence on the appearance of the sections of the cord.

No central canal was present at this level but in its position there was an accumulation of gliosed tissue with a large circular clump of ependymal cells. A little lower down, the canal itself appeared, with the ependymal cells quite regularly arranged around it (fig. 18).

These primary lesions gave rise to other changes of a secondary nature at their own and at other levels. A consequence of the destruction of the nuclei of the posterior columns and of the interposition of the slit was the complete absence of internal arcuate fibres in the left half of the medulla and of the median fillet on the right: this default of the fillet on the left side was very striking in all sections up to the mid-brain. At the level of the calamus, the area from which the fillet had disappeared seemed to have sunk, drawing forward the tecto-spinal and posterior longitudinal bundles (fig. 16).

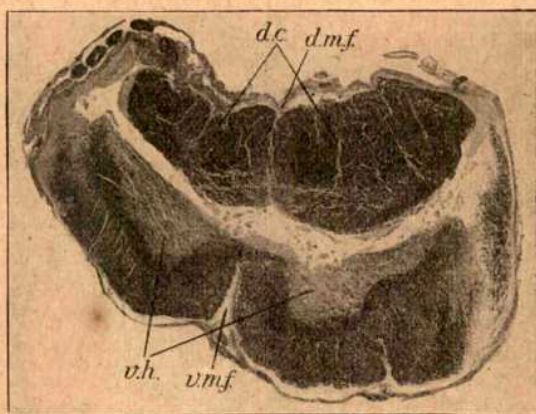


FIG. 19.—Case II. Cord at level of third cervical segment. *d.c.*, Dorsal columns; *d.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.m.f.*, ventral median fissure.

Another consequence of the interruption of the arcuate fibres was that the left half of the medulla was much smaller than that on the right; in fact the left side of the medulla as a whole was smaller.

The ventral and probably the dorsal cerebellar tracts were degenerated at this level and above. On the left side too, above the level of the lesion, the rubro-spinal tract was degenerated (retrograde).

The spinal cord.—In the upper cervical sections (fig. 19) a wide fissure ran straight right across in an arc from the entrance of the posterior roots on the

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left to the pyramidal tract on the right, reaching the periphery at both. Lying ventral to it in the middle line was the column of gliosis seen in lower medulla, with the central canal now beginning to appear in it. On grey matter only the ventral horns and the tip of the right dorsal remained. The left pyramidal tract was represented only by a few and the right pyramidal tract showed extensive degeneration; the columns of the left side were small, especially that of Burdach; on the

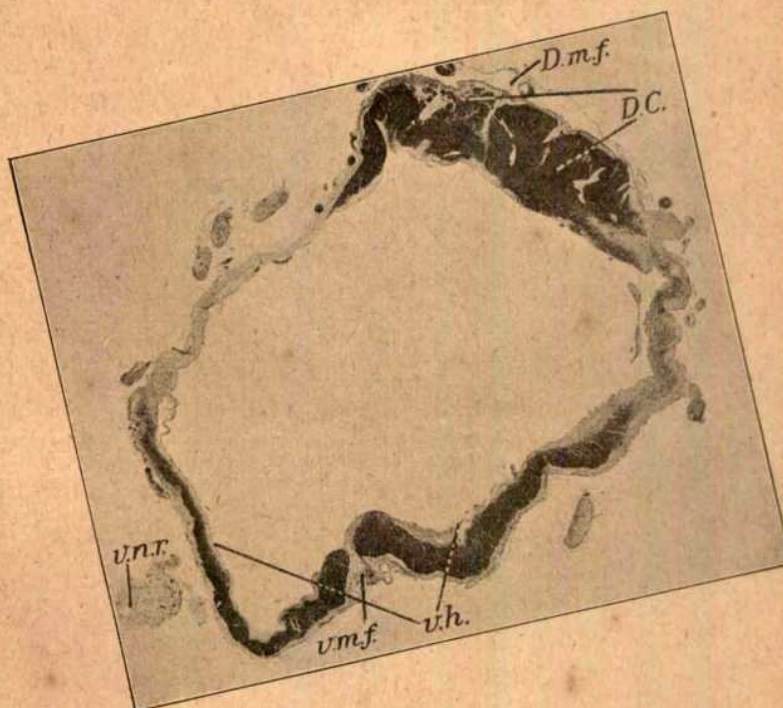


FIG. 20.—Case II. Cord at level of the cervical enlargement. *D.C.*, dorsal column; *D.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.n.r.*, ventral roots; *v.m.f.*, ventral median fissure.

side the ventral part of the column of Goll showed considerable gliosis; the ventro-median columns of both sides and the ventro-lateral of the left had undergone partial secondary degeneration.

Passing downwards, the central canal first widened and then became continuous with the cavity. It was surrounded by a large number of apparently ependymal cells, and the ependyma formed a lining for part of the ventral wall of the cavity. The cavity in the fourth cervical segment extended on both sides along the lines of the dorsal horns but did not quite reach

periphery. At the edges of the cavity large numbers of cells were present but they did not form a boundary or lining; they were apparently glial.

In the cervical enlargement (fig. 20), the sections were irregular rings, the sides of which were formed chiefly by portions of the ventral and dorsal columns; the left pyramidal tract was completely degenerated and the right extensively but not completely so. Very small portions of the ventral horns were present.

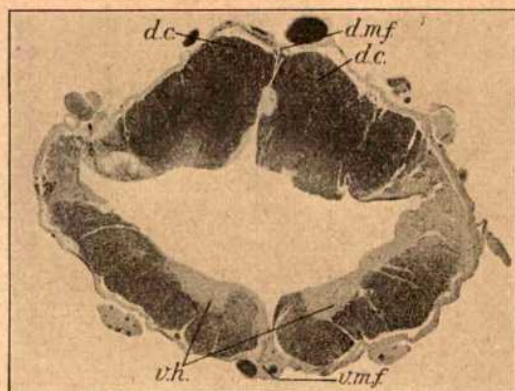


FIG. 21.—Case II. Cord in mid-thoracic region. *d.c.*, Dorsal columns; the pale oval area between them is a patch of gliosis extending from the central disease; *d.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.m.f.*, ventral median fissure.

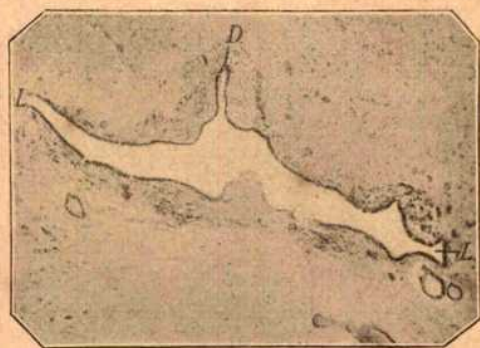


FIG. 22.—Case II. Dilated central canal at level of second lumbar segment. *D.*, Dorsal extension; *L.*, lateral extension.

Much the same may be said of the thoracic cord, but the ventral and dorsal columns were more compact, and the ring being smaller its walls were thicker. A greater part of the ventral horns persisted. More gliosed

tissue remained round the cavity, and at various levels the gliosis extended backwards between relatively healthy dorsal columns (fig. 21).

At the first lumbar segment the cavity, as has been said, narrowed quickly and appeared almost like a transversely dilated central canal. Its ependymal lining was not, however, complete, and it was surrounded by a zone of glial tissue containing a large number of cells which were ependymal in nature. The same appearances prevailed down to the third lumbar segment (fig. 22).

The outline of the cavity in the lumbar cord is particularly interesting, first, since it is similar to that of a stage of the developing canal, and secondly because a cavity of just this shape prolonged a little to one side, as it was in the first lumbar segment, would interrupt the crossing pain and temperature fibres from that side without affecting the touch fibres going to the dorsal column, and so produce a unilateral dissociated anaesthesia. A similar extension to the other side or a slight extension forwards would make the sensory loss

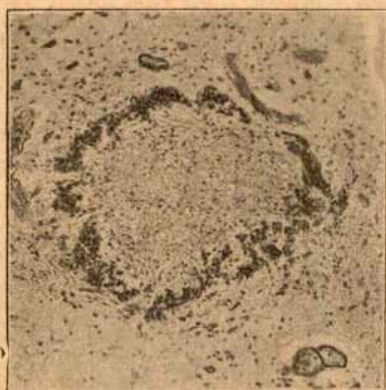


FIG. 23.—Case II. Section of fourth sacral segment; ring of ependymal cells surrounding a pencil of glial tissue. Note the clear zones around the vessels.

symmetrical. One imagines that such a lesion if placed in the cervical cord might, in the absence of any interruption higher up, be the cause of the dissociated sensory loss in one arm, which was the first symptom.

The cavity was completely closed at the third lumbar segment. In the rest of the cord a slender pencil of finely reticular substance occupied the site of the central canal, containing irregular clumps of ependymal cells; in the lowest segments these were arranged in a fairly regular ring around it (fig. 23).

Wherever gliosis or cavitation was seen, the large number and size of the vessels in and around the affected parts was noticeable; often they were actually free within the cavity. Apparently the vessels were more resistant to the process of gliosis and erosion than the nervous elements, with the result that those from the destroyed areas came together near the cavity.

The vessels which lay in or near an area of gliosis, but still surrounded by compact tissue, were usually encircled by a small pale-staining, translucent zone or by a small clear space; this appearance was best seen in the lower parts of the cord (fig. 23). This feature has been described by Schlesinger and by others.

Peripheral nerves.—Sections of the branch of the left median nerve showed no abnormality either by the Weigert-Pal or Marchi-Busch methods. The left ulnar nerve on the other hand showed gross degeneration. In sections stained by the Weigert-Pal method with van Gieson's counterstain, many of the nerve bundles showed no trace of myelinated fibres. In others there were small collections of fatty droplets which stained more deeply by the Weigert-Pal than the Marchi method; they appeared to be collections of altered myelin in the bodies of phagocytic cells and were evidence that some of the nerve degeneration had taken place at a comparatively recent date. Here and there were bundles of fibres which retained some myelin sheaths, but in most of these the proportion of fine to coarse myelin sheaths was very much greater than the normal. In some small bundles only a single myelinated fibre could be seen.

Muscles.—The flexor sublimis digitorum showed changes typical of a muscle which has degenerated in consequence of a lesion of its motor nerve. In cross sections some fibres appeared of nearly normal size, but their outline was rounded and in many the centre of the fibre stained palely. Other fibres were much smaller than normal; their shape was irregularly polygonal with rounded angles, and the nuclei of the sarcolemma sheath were increased in number and often had penetrated into the interior of the fibre. The muscle spindles and some of the nerve bundles in their neighbourhood (i.e., presumably sensory nerve fibres) appeared normal.

In longitudinal sections of this muscle it was possible to make out transverse striation in most of the fibres, but it was less well marked than normal, and in some of the fibres was almost invisible. Chains of nuclei running in between the muscle fibres were very common, and most of the fibres showed an excessive number of nuclei within the sarcolemma sheath. In many places there were clusters of darkly staining nuclei lying between the muscle fibres.

In the flexor carpi ulnaris the changes were more varied, some bundles of fibres being comparatively healthy, others presenting an appearance similar to that seen in the flexor sublimis digitorum, and still others showing a later stage of the process of degeneration. In these the muscular tissue was represented by thin fibres with no sign of cross striation, containing chains of darkly staining nuclei which constituted the greater part of the substance of the muscle fibre. Transverse sections of this muscle showed in contiguous areas these three types of degeneration, and some bundles of partially degenerated fibres were surrounded by fibres which had degenerated completely.

Here, as in the flexor sublimis, the muscle spindles were healthy.

RELATIONSHIP OF PATHOLOGICAL ANATOMY TO SYMPTOMS.

With such extensive destruction it is almost impossible to draw conclusions as to the causation of symptoms. A suggestion has been made already to explain the unilateral sensory loss by which the disease first manifested itself, but at the stage at which the patient died many pathological factors were at hand to account for her almost complete anæsthesia: as interruption of the spinal commissure throughout the cord, destruction of the dorsal root zone, lesions in the dorsal columns or their nuclei, and possibly destruction of the left spino-thalamic tract.

The weakness and wasting of the muscles of the neck and upper limbs, and the trophic disturbances in the latter, are explained by the extensive destruction of the ventral horns in the cervical and first thoracic segments. The spastic paralysis of the lower limbs was obviously due to the degeneration of the pyramidal tracts.

The dysarthria must be associated with the partial destruction of the left vagal and hypoglossal nuclei.

The complete sensory loss on the left side of the face and absence of the left corneal reflex may be referred to the lesion of the descending root of the left trigeminal nerve; that sensation was lost on both sides on the scalp and forehead considerably earlier than round the nose and mouth is explained by the fact that the descending fibres of the first division of the trigeminal nerve end at a lower level than those of the second and third divisions [11] [14]. It is stated that the fibres of the first division lie ventro-medial to those of the second and third divisions, and in sections just above the lesion the more ventrally placed fibres were pale, especially on the left side.

The smallness of the pupils and the partial ptosis of left upper eyelid are accounted for by destruction of the sympathetic centres in the cervical or upper thoracic cord.

The nystagmus is not so easy to explain. Liedler [7], from pathological and experimental evidence, concluded that nystagmus in syringobulbia is due either to a lesion of the descending vestibular nucleus of one side, or to interruption by the fissure of fibres passing from this nucleus to the posterior longitudinal bundle of the opposite side, and his view has been supported by Levy-Suhl [6]. In this case, however, no lesion of the descending vestibular nucleus was seen, and although a careful examination revealed no difference between the posterior longitudinal bundles, some of the fibres passing to them from the left vestibular nucleus must have been interrupted.

A comparison of these two cases from the pathological aspect reveals radical differences in some respects in spite of a close similarity in others.

The most striking contrast is in the relationship of the cavitation to the process of gliosis. In Case I there was much more gliosis than cavitation. For example, the lesion in the medulla appeared to be almost altogether due to gliosis, and very little cavity formation had taken place in that region. And in the cord also the amount of gliosis was everywhere much more extensive than the cavity, which, over almost the whole of its extent, was bounded by a thick wall of glial tissue. In Case II, on the other hand, the most prominent feature was the cavitation. In the medulla relatively little gliosis was seen, and, although lower down in the cord isolated areas of gliosis were present, they were small and insignificant in comparison to the size of the cavity.

This pathological difference may be correlated with the clinical histories: in Case I the morbid process ceased to progress about twenty years before the patient's death, for which it was scarcely responsible; whereas in Case II it continued active, rendering the patient gradually more helpless.

With the scanty knowledge that we possess as to the nature of the pathological process at work in this disease, the relationship of cause and effect cannot be definitely stated; but certain features presented by these two cases suggest a possible explanation of the arrest of the disease in the first case.

It has been noted that in Case II the ventricles were somewhat distended, the cervical cord swollen to considerably above its normal size, and the central canal in the lumbar region much dilated. In Case I, on the other hand, there was no evidence of hydrocephalus, but the iter of Sylvius was unusually large, and gave the appearance of having shrunk to the shape it presented in cross section during the process of fixation. Further, the thick concentric cuff of glial tissue which surrounded the cavity in the lower cervical and dorsal regions of the cord conveyed the impression that it had been formed in response to some tension or pressure from within the cavity. There is thus in both cases evidence that the cerebrospinal fluid in the ventricles and central canal of the cord was under abnormally high pressure, and that this was one of the factors leading to cavitation in the medulla and cord. In Case I either this pressure had fallen, or the glial tissue surrounding the cavity had become firm enough to withstand the destructive effects of the increased pressure.

It is usually taught, and is probably true, that the process of gliosis in syringomyelia is primary, and that it is the breaking down of the new-formed glial tissue which is responsible for the cavitation in the cord. But it must be remembered that glial tissue is in all probability endowed with a very slow rate of growth, and that although in the earlier stages of this process it is extremely fragile, in the later stages it is probably firmer than normal nervous tissue. Therefore, if the destructive process ceased for a time, the glial tissue might become firm enough to resist any further cavitation.

In Case I it is possible (and an examination of the cervical region of the cord bears out the suggestion) that the fluid had formed a channel by which it could escape into the subarachnoid space, and that the formation of this channel coincided with the arrest in the progress of the disease.

The association of syringomyelia with symptoms of increased intracranial pressure, such as headache and vomiting, has been observed by many authors. In some such cases the post-mortem examination has shown the existence of internal hydrocephalus. Such a case has been described by Grund [1]. This patient, the mother of four healthy children, commenced at the age of 24 to have headaches, which continued for nine years without the development of any other morbid symptoms. A year before her death they became worse, and were associated with giddiness and vomiting, and a little later weakness of the arms and paraplegic symptoms were added. Death occurred with Cheyne-Stokes respiration; indeed the whole symptomatology of the case suggested the diagnosis of intracranial tumour. The post-mortem examination, however, revealed no neoplasm, but hydrocephalus associated with syringomyelia and syringobulbia.

Hassin [2] has drawn attention to the increased pressure of the fluid within the cord in cases of syringomyelia. In such a case observed at operation the distended cord filled the theca, and no pulsation was seen in it. A slit made into the cord released clear fluid under great pressure and the pulsation in the cord was restored. In commenting on this case he makes the suggestion that the thickening so constantly found in the walls of the vessels in and around a syringomyelic cavity is a process of compensation for the increased pressure outside them.

The conception that increased intracranial pressure transmitted to the cerebrospinal fluid may be a dominant factor in the causation of syringomyelia is in some ways allied to the well-known theory of

Langhans [5]. He observed in four cases the association of syringomyelic cavities in the cord with tumours in the posterior cranial fossa, and considered that the latter by compressing the vertebral veins led to venous stasis and oedema in the cord, with consequent distension of the central canal and disintegration of the grey matter. This theory serves to explain not only cases such as those which Langhans studied, but also those in which cavities develop in the cord below the level at which it is compressed by a tumour.

And it is possible that a similar venous stasis may occur in the cases in which hydrocephalus is associated with syringomyelia, for the increased intracranial tension may push down the lower part of the cerebellum through the foramen magnum and thus compress the vertebral veins. A pressure cone of this kind was described by Grund [1] in the case he recorded, but it was probably a terminal phenomenon. It seems, however, unlikely that in the classical slowly progressive form of syringomyelia there is sufficient venous stasis within the cord to lead to cavitation. Nor is it common to find such cavitation in cases of cerebral tumour or hydrocephalus. Therefore, while it is possible that venous stasis may be one of the factors in the causation of syringomyelia it cannot be the chief or even an important one in the majority of cases.

Meningeal and arterial disease, by diminishing the blood supply to the central parts of the cord, may undoubtedly be the cause of cavitation in some cases. But in both our patients symptoms commenced before the age of twenty, and at the necropsy there was no evidence of meningeal thickening or arterial disease, except in relation to the cavities in the cord.

But there is evidence of another and probably more important aetiological factor in both of these cases, namely, a congenital instability of the glial tissue in the regions which the central canal of the cord occupies during foetal life. In both cases the lesion in the dorso-lateral part of the medulla corresponded fairly closely to the lateral wing of the cavity which is formed during the primary flexure of the neural tube in this region. And in both cases there was also a ventral extension of the fourth ventricle similar to what is present before the fusion of the basal laminae.

In the cervical cord in Case I the central gliosed area closely resembled the shape of the foetal central canal, and lower down in the cord this area corresponded to its ventral and dorsal extensions. In Case II the central canal in the lumbar cord was an approximate

reproduction of the foetal canal, except that an ingrowth of glial tissue had replaced the ventral extension between the basal laminae. Other considerations, such as the abnormal shape of the head, which was present in Case II and which has been described in other cases, emphasize the probability that the disease has a congenital origin.

It is difficult to explain the origin of the cavitation in the ventral part of the medulla in Case I on any of these theories. The clinical record suggested that this occurred at an early stage of the disease. In fact diplopia from weakness of the right sixth cranial nerve was the earliest symptom. Cavitation in this region is not common in syringobulbia, but has been recorded by Krauss [8], Raymond and Philippe [8], Rosenblath [10], Wilson [13], Grund [1], Spiller [12], and Rhein [9]. In the case described by Krauss the cavity lay, as in Case I, between the olive and the inner accessory olive, destroying the fibres of the hypoglossus. And in several of the other cases the cavity followed more or less exactly the line of this nerve.

An examination of the development of the hypoglossus reveals the fact that at an early stage of development the nucleus of the nerve lies relatively much nearer to the ventral surface of the medulla than it does at maturity. Several tract systems come later to lie ventral to it, notably the pyramid, the olivo-cerebellar system and the median fillet. The hypoglossal nucleus is thus shifted dorsalwards and its root fibres come to lie between the olive with its transversely crossing fibres to the cerebellum, and the two longitudinal tracts which constitute the pyramid and the median fillet. The arrangement of these tracts and the dorsal migration of the hypoglossal nucleus may make the line of its fibres a zone of lowered resistance, or of unstable cellular equilibrium, and so may lead to cavitation in the few cases in which this occurs.

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A STUDY OF THE CEREBRAL FIBRE SYSTEMS BY MEANS
OF A NEW MODIFICATION OF ANATOMICAL METHODS.
THE LATERAL WALL OF THE THALAMUS AND THE
SAGITTAL PORTION OF ITS CEREBRAL FIBRE SYSTEM.

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THE amount of knowledge accumulated respecting the functions of the nervous system, in so far as those functions manifest themselves in movements on the part of the organism, is very large. A great number of most complicated phases of normal and abnormal behaviour have been correctly observed and are clearly understood. Yet our knowledge respecting the essential structures underlying such phases of behaviour remains small in amount and indefinite in quality. The diagrammatic and semi-diagrammatic representations of the arrangement of a great number of nerve conduction pathways, current even in the best publications on the subject, testify to the scantiness of a knowledge gained by distant and indirect methods of observation. As a matter of fact, a number of such diagrams rest upon pure hypotheses which, in their turn, have been deduced from certain kinds of behaviour.

Even our best method for the study of continuous pathways in the central nerve system, the so-called Marchi degeneration method, has its peculiar limitations. From the experimental application of this method man is rigidly excluded. Yet similar as is the basic plan of structure of the nervous system in all vertebrates, the human nervous system differs in many respects from the brain of even the highest anthropoid ape. In proportion to the size of the body the human brain is very much larger in bulk; and this increase in bulk implies both a vastly increased number of neurons, and a vastly increased complexity in their arrangement.

The study of the conduction pathways in the human brain by means of the Marchi method requires a rather involved combination of favourable circumstances. The lesion must be very small; the person must die within a period of some three weeks after the occurrence of the

lesion, and there must be an opportunity for an autopsy. Such a combination of circumstances is sufficiently rare to make this excellent method of very limited application.

The opportunities for study offered by old lesions, in tissue stained by the Weigert method, are, of course, very much greater. Yet whatever stain is employed, the current methods of sectioning the tissue make its subsequent investigation a matter of extreme difficulty, and the results of such a study to a great extent uncertain. Except in a few situations the fibre tracts in the brain do not pursue any direction for more than a fraction of a millimetre. Owing to their sinuous course they are cut obliquely or irregularly no matter in which direction the section is made. What one sees in the best Weigert preparations of the brain is a beautifully variegated and almost hopeless picture constituted of millions of dots and streaks.

Careful dissection of properly hardened tissue, although the oldest, still remains one of the best methods at the disposal of the anatomist. In the dissection of the brain, however, one meets with certain dangers and difficulties. The chief danger is the fallacy into which one is almost certain to be led by habitual attempts to make microscopic deductions from macroscopic appearances. The greatest difficulty is that of retaining good records of the successive steps in the dissection. In the best photographs of such preparations most of the fine detail is utterly lost, while good drawings are rare, expensive and time-consuming. Yet unless many of the consecutive steps in the dissection of any one specimen are correctly recorded for subsequent study, criticism and comparison, the method, relatively crude as it is to begin with, must remain of correspondingly small value.

The modification of current anatomical methods to be described, obviates many of the difficulties and increases the certainty with which fibre tracts may be traced in the central nervous system. By means of current methods, the direction of lines and surfaces is inferred from the observation of points; by means of the modification to be described, points, lines and surfaces are directly observed. By the employment of this modification it has been possible to view a very large portion of an entire cerebral fibre system, such as the thalamic, pallio-pontine and others, each in a single section under the microscope; and to trace with comparative ease and exactness the course of bundles that have hitherto been represented only schematically.

METHOD AND GENERAL TECHNIQUE.

The method consists of two processes: (1) longitudinal sectioning and (2) serial dissections.

(1) Longitudinal sectioning is a method of preparing serial microscopic sections of any size in the plane of the course of a fibre-tract, or of an entire cerebral fibre system. The general technique will be given in this place, and the special steps to be taken in the preparation of sections of very large and complicated fibre systems will precede the description of each system.

The method may be employed in connection with a number of the ordinary stains and with either normal or pathological tissue.

(a) The particular fibre bundle or sheet is dissected out along the apparent course of its fibres. In well-fixed tissue such dissection is made comparatively easy by the use of the right kind of tools. In addition to the knife and scissors, the tools employed in the present work were small, spade-like, blunt-edged glass chisels, curved at an angle of about 100° at their ends. Such chisels are easily made in the Bunsen flame, and are very smooth and keep clean. Their curve enables one to get under the thinnest strand of fibres and to lift it out of its bed by leading the instrument along its under surface in the line of cleavage of the fibres. Such instruments, too, make it possible to reach fibre-strands in places which are inaccessible to a straight instrument without a serious distortion of the parts, such as the depth of the posterior and inferior extensions of the lateral ventricle.

(b) The detached strand is marked so that the relations which its several parts bore to the bed from which it was detached can be determined. A rough drawing accompanied by legends serves the purpose.

(c) The piece of tissue is placed on a numbered glass slide, the side in contact with the glass being carefully recorded. A pad of absorbent gauze, uniform or varying in thickness according as the tissue is of the same thickness throughout its extent or not, is placed upon the specimen, and is covered with a second glass slide of the same size as the first. This package is now tied with a strong string, the degree of pressure exerted in tying being such as to ensure the uniform application of the tissue to the glass slide on which it rests.

(d) If the Weigert-Pal stain is to be employed, the package is immersed in one of the mordanting solutions. There it remains for three or four days, or long enough for the tissue to retain its flat shape when the package is untied. It is then taken out of the solution,

untied, and the top slide and the gauze pad removed. The strand of tissue is lightly fastened with a thread to the slide on which it rests and immersed once more in the mordanting solution, where it remains for the necessary length of time.

If it is intended to use a stain which requires no preliminary mordanting of the tissue, the process of flattening it permanently may be accomplished by the use of alcohol or of any other fixative agent.

• (e) When the mordanting is completed the glass slide with the piece of tissue tied to it is removed from the solution, washed, and treated with the alcohol and the ether solutions in the usual way employed in the preparation of Weigert-Pal celloidin sections.

(f) A glass slide is covered with tin (not lead) foil, and fastened to it by bending the edges of the metal around those of the glass. The tin-foil should be about 0.5 mm. in thickness. Such foil may be spread over the glass so that its surface is perfectly smooth and even. An attempt to use the ordinary very thin foil is almost certain to result in the failure of the subsequent procedures. The tin-covered slide is placed in a celloidin solution with the tin up. The slide bearing the tissue is removed from the alcohol-ether solution; the thread which holds the tissue to the glass is untied, and the tissue is gently pushed off the old slide and placed on the tin surface of the slide in the celloidin solution.

The vessel containing the celloidin solution should have a flat bottom, and it should rest upon a horizontal surface. The amount of solution in the vessel should be such that when it reaches the necessary final consistency its surface should rise above the embedded tissue for a height of about 3 or 4 mm.

(g) When impregnation and embedding is completed, a cut is made through the thickness of the celloidin, passing around the tin-covered slide. A convenient instrument is passed under the edge of the slide, it is lifted out, and its celloidin surface is fastened to a wooden block in the usual way. With the block resting on a table, the relations of the whole are then the following, from top to bottom: glass slide, tin-foil, tissue, a generous layer of celloidin, wooden block.

The edges of the tin are now bent away from those of the glass slide and the latter is removed. An edge of the tin is then held against the side of a pencil, which is rolled over the surface of the embedded tissue in such a manner that it becomes wrapped in the tin-foil. The metal is thus removed from the adjoining tissue, leaving behind a surface as straight and polished as a mirror.

The preparation is treated with alcohol or with cedar oil, in the usual way.

(h) The block is adjusted in the microtome in such a manner that the first cut will shave off a complete section. This is relatively easy since the tissue presents a perfectly even surface. In the present investigation it was found convenient to set the long diameter of the block as parallel as possible to the edge of the microtome knife; on the whole, therefore, the sections were in the same plane as, and more or less at right angles to, the apparent course of the fibres. The layer of celloidin between the tissue and the block permits the sectioning of the entire piece without waste. In this manner it was possible to produce longitudinal sections of strands of tissue 10 cm. long, 3 or 4 mm. in width and less than 1 mm. in thickness.

If the apparent course of the fibres in the tissue is not their true course, the fact is immediately discovered in the stained section. In a true tract the fine bundles of fibres may be followed in one and the same section in their entire length by merely moving the slide along the platform of the microscope. When a bundle leaves the main tract its deviation in a large field of uniformly parallel bundles is detected with the greatest ease. Moreover, in such sections perforating bundles are seen with a remarkable degree of definition, the cross-sectioned areas standing out prominently amid a field of longitudinal fibres. An example of such a perforating bundle is the auditory tract, which is cut across in the sagittal sections of the lateral portion of the thalamus. Those who have looked for this tract in normal Weigert-~~stained~~ preparations generally fail to identify it.

(2) In the microscopic preparations just described, the course of the fibre-tracts is observed in the two possible directions on a plane surface. Thus, in the illustrations which follow, the direction of the fibre-bundles is either up and down, or from before backward, or partly the one and partly the other direction. In order to leave as little as possible to the uncertain processes of deduction, the third direction was supplied by Serial Dissections.

For these dissections formaldehyde-hardened tissue was used. After thorough fixation the brains were removed from the formaldehyde solution, wrapped in towels and placed in loosely-covered jars. After two or three months the brain-tissue, but slightly shrunken, became sufficiently tough to permit the most detailed dissection.

A record of each step in the dissection is obtained by pouring on the preparation molten wax which, on cooling, furnishes a mould into which is poured plaster of Paris. When the plaster has set the wax is melted out. In this way a series of faultless reproductions of the

several steps in the dissection of the hemisphere is obtained. The series may be as large as the investigator pleases. In the present study seventy-eight casts were made of as many steps in the dissection of one hemisphere; fifty-seven of another; only ten of a third; and so on. For the study of the relations of the parts, and for comparison with the microscopic sections, such a series is invaluable. The moulding and the casting require but little time and skill. The wax never sticks to the damp brain-tissue, and projecting parts are pulled out of the mould with little difficulty.

SPECIAL TECHNIQUE FOR THE PREPARATION OF LONGITUDINAL
MICROSCOPIC SECTIONS OF THE SAGITTAL PORTION OF THE
THALAMIC RADIATION.

A curved instrument is entered between the corpus callosum and the cingulum, and the entire cingulum convolution, from the paraterminal body to the hippocampus, is removed. The association sheets between the cingulum and the other convolutions are next cleared away, until the callosal fibres are seen covering the entire mesial aspect of the hemisphere as far below and behind as the parieto-occipital and anterior calcarine fissures.

The septum lucidum is removed, the anterior pillar of the fornix cut as low down as possible, and the band of the fornix pulled away from around the thalamus. Below that band is torn off, together with the hippocampus and a part of the uncus, a short distance in front of the receding angle of the temporal ventricle. The association-sheets in the small sulci of the cuneus are cleared away. The floor of the anterior and posterior limbs of the calcarine fissure is cut through. The lateral ventricle is thus everywhere opened.

The superficial fibres on the dorsal and anterior surfaces of the callosal band—the fibres which face the antero-superior border of the hemisphere—are lifted up strand after strand and pulled off the mesial aspect of the hemisphere which they cover. This is continued until the thickness of the cut border of the corpus callosum is reduced to about one-half. At this stage it is found that the fibres of the callosal band, when pulled upon, break off easily at their point of contact with the hemisphere. These are the perforating fibres, and the fact that they have been reached is an indication that above the line of their entrance into the hemisphere the thalamic fan has been exposed on the mesial surface.

The ventricular ependyma is peeled off everywhere, except in the

groove between the corpus callosum and the caudate nucleus and in that between the latter and the thalamus. In the former groove the ependyma is strongly adherent to the fasciculus subcallosus, a part of which may be torn away by an attempt to expose it; in the latter the ependyma is as strongly adherent to the stria terminalis.

In the posterior and inferior extensions of the ventricle the removal of the ependyma brings to view the fibres of the tapetum. This covering must be lifted with great care, especially in the inferior horn where it is very thin. Lateral to this layer, the entire expanse of the ventricle, except the narrow space around the thalamus which is occupied by the tail of the caudate nucleus, is carpeted by the fibres of the thalamic fan.

The instrument is now inserted into the substantia nigra and the thalamus separated from the fibres of the pes pedunculi. With the fan of the peduncular radiation as a lateral guide, the sagittally placed sheet of thalamic fibres is easily separated from the mesial aspect of the hemisphere in the frontal, parietal, and occipital regions. The expanded portion of the anterior commissure is a lateral guide in the separation of the thalamic sheet in the anterior half of the temporal ventricle. Lateral to the thalamic fibres in the posterior portion of the temporal and the lower half of the occipital ventricle is a layer of fibres converging towards the globus pallidus, and from this layer, too, the thalamic sheet is separable with ease.

The protruding mesial portion of the optic thalamus is now gradually torn away in the line of cleavage of the fibres, leaving a thickness of 5 or 6 mm. of its lateral wall.

The circumference of the large sheet thus obtained is serrated above, the serrations corresponding to the gyri and sulci at the superior border of the hemisphere. Below the circumference corresponds behind to the lower lip of the calcarine fissure; in front to the outer or lower portion of the hippocampal convolution. Still more anteriorly the gap in the outline of the circumference corresponds to the horizontal fissure, in front of which is the gyrus rectus.

The surface of the sheet which corresponds to the mesial aspect of the hemisphere is placed on a large slide, and the preparation treated as described under the heading of General Technique.

THE LATERAL WALL OF THE THALAMUS AND THE SAGITTAL PORTION OF ITS CEREBRAL FIBRE SYSTEM.

Fig. 1 was prepared practically from a single section. A few defects were corrected from four other sections. The size of these sections was nearly 13 by 9 cm. It is not possible to produce a single photomicrograph of an entire section of such size at a magnification at which the small bundles of fibres become visible. The alternative is to photograph or to draw the section in parts, and to put the fields thus reproduced together side by side in the proper order. For practical reasons the expedient of drawing was adopted. The Edinger epidiascope was used at a magnification of 25 diameters. The resulting huge drawing—1·8 by 2·3 metres—was then photographed and reduced to its present dimensions. The lines of the photograph were gone over with ink and the photograph bleached out.

The disadvantage of such an illustration is that although it gives a concrete idea of the general appearance of the stained section, the sharpness of its lines produces the impression of a diagram. Such an impression is true to the extent that each line in the drawing represents not a nerve-fibre, but a bundle of fibres in the section drawn. The advantages of such a drawing are the concreteness of the fairly correct idea of the appearance of the section which it furnishes, and the fact that it enables one to eliminate certain irrelevant features, such as the perforating bundles of the corpus callosum.

A number of photographs were taken from different parts of the sections employed in making the drawing, and some of these are reproduced in the illustrations. They serve the purpose of correcting the impression of the diagrammatic nature of the drawing. Such a correction is especially important in this case, since, as will be seen, the facts revealed in these longitudinal sections differ in several essential points from those of a number of investigators who based their conclusions on sections cut in the ordinary way.

In this study the Weigert-Pal stain has been used throughout. This stain furnishes no clue to the functional direction of a nerve-fibre. It is to be understood, therefore, that except where such a functional direction is explicitly stated, *it is nowhere implied in the forthcoming descriptions.*

The main bulk of the thalamic radiation has the general form of a fan open for about 300 degrees of a circle. The gap in the circle is the horizontal fissure. This fan is placed, on the whole, in a sagittal

direction. A detailed account of its relations to adjoining structure will appear in a special paper.

The division of the thalamic radiation into several peduncles has no anatomical foundation. Dejerine [4] called attention to this fact, and other investigators agreed with him that the term "peduncles," in connection with the thalamic radiation, is to be used for convenience only.

Although it is true that the bundles of fibres of the thalamic fan are nowhere separated to the extent of justifying a division into peduncles, yet the several parts of the fan are each marked by certain characteristic features. These will be described as they appear when the thalamic radiation is viewed on a sagittal plane.

THE TEMPORAL THALAMIC RADIATION.

This does not include the auditory tract, which, in these sections, appears as a bundle of transversely cut fibres (fig. 1, IV).

The anterior portion of the temporal thalamic radiation has been described by Arnold [1], and has since been known as the temporo-thalamic fasciculus of that author. Since its fibres are spread out over the wide expanse of the wall of the temporal ventricle, however, this part of the radiation can hardly be called a fasciculus. In their course these fibres describe a series of curves which cannot be entirely explained by the curved lateral outline of the ventricular wall. From their junction with the postero-inferior portion of the thalamus, they proceed forward in the lateral wall of the temporal cavity. At varying distances from the receding anterior angle of the ventricle the fibres curve mesially within the floor, and the most anterior reach the mesial wall. All these turn backward, some within the floor, others within the mesial wall, and proceed in a posterior direction (fig. 1, I). The reason for this singular curvature of the fibres is probably to be found in the forward growth of the temporal lobe after the thalamic elements in it have been laid down, a probability which awaits corroboration at the hands of the embryologist.

In the long posterior part of their course the temporal fibres are arranged in parallel, rather coarse bundles, which are similar in appearance to those of the occipital radiation (fig. 1, II).

Before their junction with the optic thalamus, for a space of about 3 mm., the temporal fibres pass through the striate body, through the tail of the caudate nucleus. Within the substance of the latter they

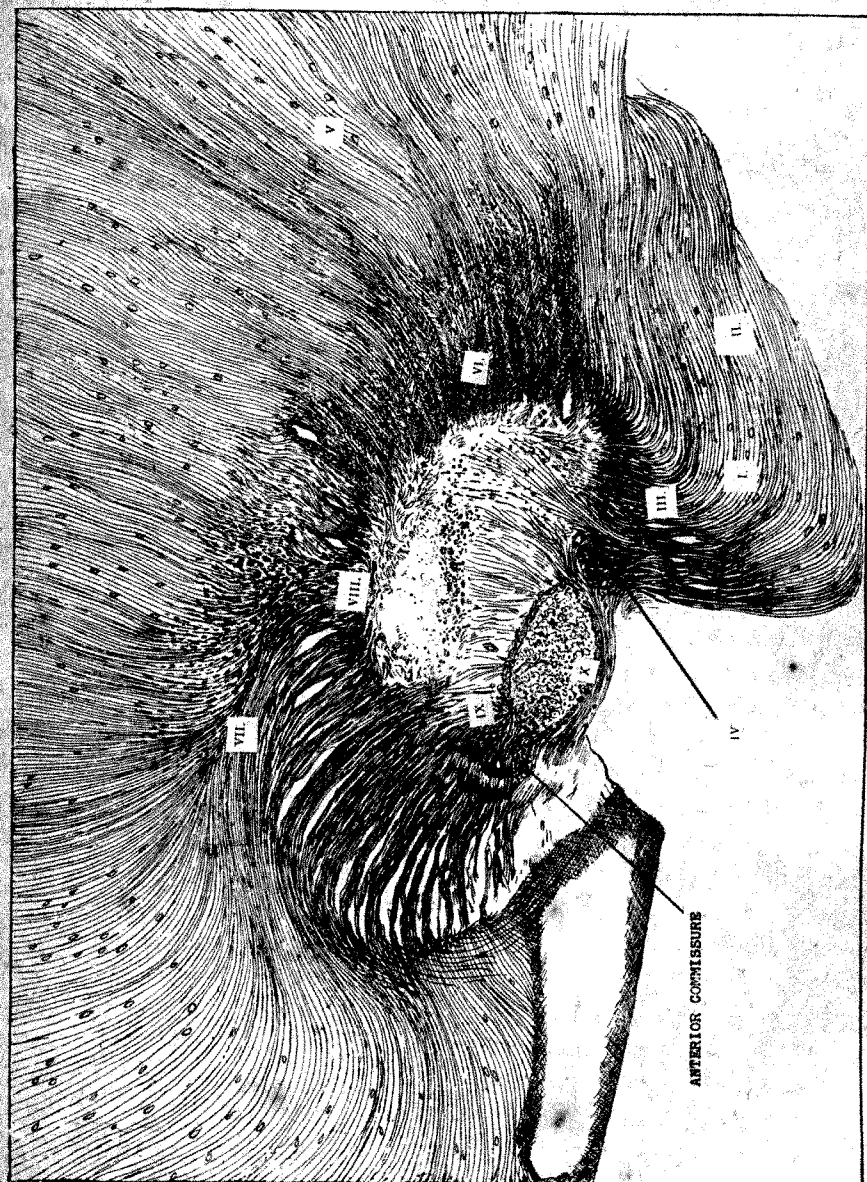


FIG. 1.—A drawing of the lateral wall of the thalamus and the sagittal portion of its cerebral fibre system.
Details $\times 25$.

are arranged in the form of flat bands, alternating with wide spaces occupied by the tissue of the striate body (fig. 1, III). The adjoining bundles show little tendency to interchange strands of fibres, as is the case in similar situations elsewhere, or to break up to any large extent into a brushwork of fibres similar to the brushwork to be described in connection with the occipital radiation. A number of fibre-bundles continue indeed distinct and parallel in an upward and backward direction until they have reached well into the outer middle portion of the nucleus of the pulvinar and the adjoining part of the lateral nucleus. That projection fibres from the temporal pallium stand (in the cat) in connection with the ventral region of the lateral nucleus, has been shown by E. Sachs [25] by means of experimental lesions. The nearly vertical course of the temporal fibres in the pulvinar gives that nucleus its characteristic streaked appearance.

Within the body of the thalamus most of the temporal fibres are situated immediately behind the auditory tract. This tract passes from side to side and is, therefore, cut across in these sections (fig. 1, IV). A smaller number of the temporal fibres, however, are placed in front of the auditory bundle, and are there intermingled with the fibres of a tract situated beneath the subthalamie body, which will be described later.

THE OCCIPITAL THALAMIC RADIATION.

Two characteristics distinguish this portion of the thalamic system. For the greater part of their length the bundles, neatly arranged and parallel (fig. 1, V, and fig. 2), are coarser in texture than the other fibre bundles of the thalamic system. At a distance of about 2 cm. from the posterior surface of the thalamus, they begin to break up into their constituent fibres, appearing at first like a row of stiff feathers, but gradually, as they approach the thalamus, assuming the form of a soft, matted brushwork, with the general direction of the filaments toward the thalamus (fig. 1, VI). In the study of the fibre systems in the longitudinal sections, this phenomenon will be encountered over and over again. It is always significant of the proximity of the fibre bundles to the nuclear mass in which they disappear. As this feature is rather conducive to hasty deductions respecting the beginning or the ending of a fibre tract, it is important to visualize it and to understand it.

If the handle of a camel's-hair brush be taken to represent a compact bundle, then the brush itself will represent the part of the bundle



FIG. 2.—The occipital thalamic radiation: $\times 27$.

where its fibres are spread more widely apart. If a number of such camel's-hair brushes, lying side by side, be embedded in paraffin or celloidin and then sectioned in the longitudinal plane, their appearance in each section will approximate that of the nerve bundles in fig. 1, VI.

In the neighbourhood of a nuclear mass in which a fibre tract begins or ends, its constituent fibres, gathered into compact bundles, must spread out. For this there are two reasons. One is that each cell is thicker than the fibre with which it stands in connection, and the entire nuclear mass, therefore, occupies a wider space than does the tract of fibres which it sends out or receives. The other is a rule which appears to hold good throughout the nervous system, central as well as peripheral, that there is a continual interchange of fibres between the adjoining bundles of a tract. That this arrangement holds good in the peripheral nerves, has been abundantly proved by the researches of Sherren [27], Heinemann [11], Langley and Hashimoto [13], McKinley [15], and a number of others. A careful inspection of the cerebral tracts shows that the finest parallel bundles which appear to retain a uniform thickness for a long part of their course, continually anastomose by means of very fine fibres, and that the whole tract is in reality a plexus of extreme intricacy. Owing to this it must be true that the mutual relations of the fibres in a nerve tract in the proximity of the nucleus in which it disappears are not the same as the mutual relations of the cells in the nucleus to which the fibres respectively belong. Thus of two fibres placed on the right of a nerve tract, one may pass to a cell on the right, the other to one on the left side of the nucleus. Hence the appearance of a matted brushwork of fibre bundles in the proximity of a nuclear mass to which they belong, seen in the longitudinal sections.

The phenomenon described, however, needs further investigation. It may be pointed out that in the neighbourhood of nuclei which are known to be efferent, such as the cranial and spinal motor nuclei, the emerging nerve-tracts are at first composed of parallel or converging fibres. In such nuclei each cell sends out but one nerve fibre, and these fibres then converge to form a nerve tract. There appears to be no reason for any matting of the fibres of an efferent bundle in the proximity of its nucleus, and none is observed. In the case of a tract near its nucleus of termination, however, the circumstances must be different. The fibres of that tract have changed places repeatedly, and in the neighbourhood of its nucleus each small bundle must break up into its constituent fibres, and the fibres must break up into thinner

fibrillæ, in order that each may come into relation with a number of cells or cell processes in different parts of the nuclear mass. Such a tract might be expected, therefore, to have the appearance of a matted brushwork near the nucleus which it is to enter. It may be said that for the same reasons a tract containing both afferent and efferent fibres might be expected to present a mixed appearance near the nucleus in which some of its fibres originate and in which others end. Such a mixed appearance should be clearly observable in sections cut along the course of such a tract. In the sections examined in connection with the present study, however, nothing but a mere suggestion of this appearance has been observed, and on that no conclusion can be based. The only certainty so far reached is that in the neighbourhood of the nuclear aggregate in which the fibres of a cerebral tract gradually disappear from view, the bundles of that tract are always seen in Weigert-Pal sections to assume the form of a matted brushwork. When examining the course of the prefrontal part of the thalamic radiation an opportunity will be presented for contrasting sharply the appearance of its smooth fibre-bundles near and within the thalamus with the matted brushwork of the other contingents in similar situations.

On joining the nucleus of the pulvinar the rich brushwork of fibres into which the parallel and well-defined bundles of the occipital radiation have spread out, gradually breaks up and disappears.

THE PARIETAL THALAMIC RADIATION.

In sagittal longitudinal sections of the thalamic radiation this part always appears defective. In contrast to the pictures presented by the other contingents, that of the parietal is marred by a number of thick, short streaks (fig. 1). A certain number of fibre bundles bend away from the sagittal plane in a direction which is at first forward, upward and lateral. In their forward course these bundles contribute to the formation of the fasciculus subcallosus which will be described later. They then proceed further laterally, in an upward and backward direction. Owing to their lateral inclination they are cut in short strips in these sections. Their appearance is distinct from the rest of the parietal bundles; they are very much thicker and converge below at an unusually large angle, between 45° and 90° .

The general backward sweep of the parietal radiation, as well as the number of laterally inclined thick bundles which it contains, demar-

cate it rather sharply in front from the frontal portion of the thalamic fibres. Behind, however, it merges gradually into the occipital radiation.

At a distance a little over 1 cm. from the optic thalamus, the fibres of the parietal radiation become aggregated into rounded bundles some 2 or 3 mm. in thickness. The spaces between these bundles are occupied by the substance of the striate body, through which they pass on their way to the thalamus. These bundles will be further considered in the next section.

THE FRONTAL THALAMIC RADIATION. THE FASCICULUS SUBCALLOSUS.
THE STRIA TERMINALIS. THE FASCICULUS THALAMO-TEMPORALIS
ARCUATUS.

In dissections of the body of the lateral ventricle, a bundle of fibres may be seen lying in the groove between the head and body of the caudate nucleus below and the corpus callosum above (fig. 3). This bundle is most prominent over the dorsal portion of the head of the caudate; it thins out over the body of that nucleus and disappears at the beginning of its tail. In certain specimens it attains a thickness of 3 mm. from above downwards at its thickest part.

The extent to which the current methods of sectioning the brain are conducive to error is well illustrated by the conclusions reached respecting the nature of the subcallosal bundle by universally recognized authorities. One conclusion is that it serves as a connection between the cerebral cortex and the caudate nucleus; another, that it is an association tract between different parts of the caudate nucleus; a third, that it is a fronto-occipital association tract.

H. Sachs [26] states: "The most important bundle which unites the corpus striatum with the grey cortex . . . is the fasciculus nuclei caudati. This bundle accompanies the caudate nucleus, running parallel with it . . . on the lateral wall of the lateral ventricle. . . . Lateral to this bundle is the corona radiata of the internal capsules. Posteriorly it diminishes in proportion to the diminution in thickness of the caudate. . . . from the bundle fibres pass . . . and become lost there. It appears that this bundle . . . coming from the frontal and the parietal . . . from the insula."

Koelliker [12] sums up his conclusion . . . accompanies the caudate nucleus . . . extent, ventral to the corpus callosum . . .

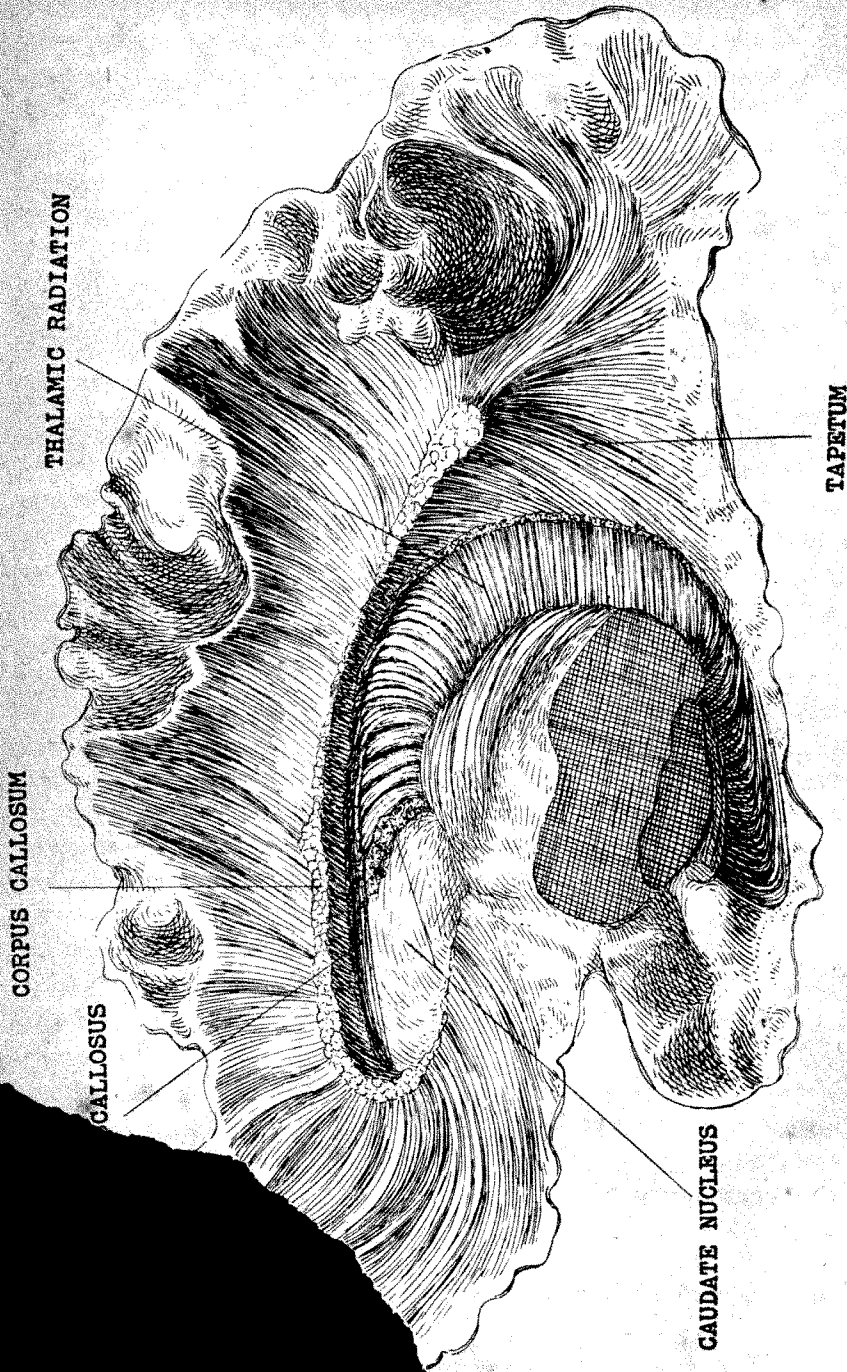


FIG. 3.—A drawing of a cast of a dissection on the mesial surface of the hemisphere. The body and tail of the caudate nucleus have been scraped away to expose the relations of the subcallosal bundle to the frontal and parietal bundles of the thalamus. A part of the tapetum has been cut away to show the course of the temporal and occipital thalamic bundles.

wall of the lateral ventricle. It diminishes in cross section from before backward. . . . Fibres enter the nucleus caudatus, where they become dispersed. . . ."

Edinger [6] devotes considerable attention to this bundle. "In mammals," he says, "there exists a small fibre tract which passes along the entire extent of the nucleus caudatus. It begins in front at the head of the ganglion as a few fibres which appear to come out of the head itself. This tract increases in size more and more posteriorly for a certain distance, then becomes smaller, in consequence of the slenderness of the tail of the nucleus. . . . The bundle lies in the angle between the nucleus caudatus and the roof of the ventricle; the fibres of the corpus callosum radiate over it. The fibres of this bundle appear to come from the nucleus itself and to return into it again. This is called the association bundle of the nucleus caudatus; but I cannot separate it sharply from the fronto-occipital association bundle which lies close to it."

Bechterew [2] is very emphatic in his statement that this bundle consists of fibres connecting the cortex with the caudate nucleus. He states that degeneration of that bundle is observed principally after lesions of the frontal and parietal lobes, and to a less extent in those of the occipital lobe. After destruction of the frontal lobe it was possible to observe the degenerated area diminish from before backward, which, he thinks, points to the fact that the fibres originating in the frontal region of the cortex end in succession from before backward in the caudate nucleus. In a footnote the author cites Flechsig as being of the same opinion.

Probst [20], however, was not able to find any considerable degeneration in the subcallosal bundle in isolated lesions of the caudate nucleus. After destruction of the bundle in the anterior parietal region, the fibres degenerated in his experiments for a short distance only, and he could not follow their ends with certainty. He states, however, that more extended degeneration of the fasciculus followed deep destruction of the posterior cerebral region.

In the sagittal sections of the thalamic fan prepared by the method of longitudinal sectioning, the subcallosal bundle stands out with the greatest degree of clearness possible with the Weigert-Pal stain. With the unaided eye, as well as with all degrees of magnification, the bundles of fibres composing it can be traced from the frontal and partly from the parietal regions . . . sphere, through the substance of the



FIG. 4.—Fasciculus subcallosus, $\times 27$. Above the direction of the bundles is almost horizontal. They are plainly seen to curve down, plunging through the substance of the caudate nucleus, on the way to the thalamus.

caudate nucleus, and into the optic thalamus. Fig. 1, VII, and fig. 3, indicate the course of the fibres composing the subcallosal fasciculus.

The fact is that the fibres between the frontal regions of the cortex and the thalamus pursue a rather intricate course. From in front and above they pass at first downward and backward in a series of graceful curves; they then all turn backwards in an almost horizontal direction over the head and body of the caudate nucleus. In the horizontal part of its course the entire mass of fibres is packed into a single bundle of considerable width. At various distances from before backward this horizontal band gives off five or six fasciculi, which turn downward and plunge through the substance of the caudate nucleus to join the thalamus in the region of the stria terminalis.

A vertical or a horizontal section of the hemisphere passing through the caudate nucleus shows that no part of it is sufficiently separated from the rest of the corpus striatum to allow it to be regarded as a separate ganglion. To the anatomists who have described the subcallosal bundle the fact was well known that the existence of the caudate nucleus as a separate entity is a mere gross appearance. The form of that nucleus—a thick head in front, a body and a thin tail behind—is due mainly to the fact that from a mesial viewpoint the smaller thalamus leaves exposed a greater portion of the striate body above and in front than it does behind and below. Nor is the separation of the exposed from the concealed part of the striate body at all accomplished by the stream of fibres which perforate that body.

Even if it were true, then, that the fibres of the subcallosal fasciculus stand in connection with the cells of the caudate nucleus, it still remains difficult to understand why the fasciculus diminishes in thickness posteriorly, in proportion to the diminution in the thickness of the caudate nucleus.

A case of agenesis of the corpus callosum in the microcephalic brain of an idiot, described by Onufrowitch [19] and later by Forel [7], is responsible for a conception of the nature of the subcallosal fasciculus which still prevails. Notwithstanding the absence of the callosal band in this case, the tapetum was intact in the posterior extension of the lateral ventricle. Onufrowitch and Forel thought, moreover, that the tapetum was continuous in front with a bundle of fibres which passed between the cingulum and the caudate nucleus to the frontal portion of the hemisphere. They, therefore, concluded that the tapetum was not part of the corpus callosum, but that, together with the bundle of fibres which they saw pass to the frontal portion of the hemisphere, it

constituted a fronto-occipital association tract. They called it the fronto-occipital fasciculus and identified it with the superior longitudinal or arcuate fasciculus described by Burdach.

Muratoff [18], in his experiments on dogs, found by the employment of the Marchi method that the amount of degeneration in the bundle described by Onufrowitch was relatively small when any single cortical area was injured. He also found traces of degeneration in it in lesions of the parietal cortex as well. He, therefore, disagreed with Onufrowitch that the bundle served to connect only the two areas implied by its name, and came to the conclusion that it was too complex in nature for any specific name and proposed to call it the fasciculus subcallosus. Respecting its identity with the superior longitudinal fasciculus of Burdach, he rightly pointed to the fact that the latter association tract is situated on the lateral side of the corona radiata, while the bundle in question is to be found on its mesial side.

Dejerine [4], using the same argument as did Muratoff, points out the error in identifying the subcallosal fasciculus with the superior longitudinal fasciculus of Burdach. He agrees with Onufrowitch and Forl that the subcallosal bundle is a fronto-occipital association tract. He brings, however, a number of facts to bear upon the nature of the tapetum, showing that it does contain a certain contingent of callosal fibres.

Wernicke [28] thought that the fasciculus in question was composed mainly of the fibres of the corpus callosum, but that it also contained a certain number of fibres from the frontal lobe. He declares, however, that he knows nothing further about its course.

That the subcallosal fasciculus is composed of fibres which extend into the large areas of the frontal and parietal cortex, has already been noted. When considering the course of the prefrontal and orbital fibres it will be seen that they curve for some distance upward around the head of the caudate nucleus, before plunging through its substance. In that situation, therefore, these fibres contribute to the formation of the anterior portion of the subcallosal bundle (fig. 1).

It can be easily understood that lesions of the occipital cortex would bring about degeneration of the fibres of the tapetum, if this is constituted either in whole or in part of callosal fibres. That lesions of the parietal and frontal regions of the cortex would result in degenerations in the subcallosal bundle is also easily understood. Yet that by no means implies the continuity of the frontal and parietal fibres with those of the tapetum. The difficulty lies in the obscure space which

converges from behind forward between the posterior portion of the callosal band above and the optic thalamus below (see fig. 3). The greater portion of the lateral ventricular wall is there occupied by the tail of the caudate nucleus, above which the subcallosal bundle ends, while the fibres of the tapetum, which stream to or from the callosal band, curving around the tail of the caudate, overlap the ending of the subcallosal bundle. The suggestion of the continuity of the two is indeed strong. In any microscopical preparations where all the fibres are cut across and where all appear alike, it is quite impossible to recognize a line between the two. A lesion at this point would certainly involve both the fibres of the tapetum and those of the subcallosal band. Even some distance in advance of the ending of the bundle a lesion of the tract, by encroaching upon the closely adjoining fibres of the corpus callosum, might be followed by traces of degeneration in the tapetum on the one hand and in the frontal and parietal regions of the hemisphere on the other. In such a case, too, preparations containing vast numbers of fibres cut across must be misleading. In sections, however, where the thinnest bundles may be traced in their continuity, the posterior course of the subcallosal fasciculus is very plain (figs. 1, VII, and 4).

As to the nature of the tapetum, it is well to bear in mind that the last word has not yet been said on the composition of the corpus callosum. Hamilton [10] may have been wrong in his conclusions on its nature, but Beevor [3], who attempted to correct the error, was not altogether right. Cajal's silver impregnation sections are very convincing, and his [22] conclusion is that the corpus callosum is constituted in great part of collaterals of the projection and association fibres of each hemisphere. Roussy's [24] belief is "that a certain number of fibres depart from the optic thalamus and, by way of the corpus callosum, arrive at the cortex, and even in the thalamus of the opposite side." It is certain, too, that the corpus callosum contains a number of projection fibres of the ancient olfactory system. It must, therefore, be conceived as a commissural band which contains elements of many or even of all kinds of fibres of each hemisphere on their way to or from the opposite side. In the light of such a conception it will be readily understood how any portion of the corpus callosum may be present, though the rest be congenitally absent. If, therefore, any portion of the thalamic or the other fibre systems in the temporal and occipital regions attained a certain degree of development, the tapetum may very well have been present in the defective brain described by Onufrowitch and Forel.

The *Stria terminalis* or the *Stria cornea* is a prominent linear projection in the groove between the caudate nucleus and the optic thalamus. With certain differences in detail, it is the general agreement of Arnold [1], Meynert [16], Koelliker [12], Ganser [9], Edinger [6], Probst [21], Dejerine [4] and others, that in animals it is a fibre tract which begins in the masses of grey matter in the region of the anterior perforated space—the nucleus amygdalæ, the anterior portion of area pyriformis, the uncus, &c.—and which, after surrounding the optic thalamus, ends in the same masses again. Cajal [22] comments on the extreme difficulty of following this fibre band in man. His study of the tract in young mice has led him to the conclusion that the stria is both a commissural—by way of the anterior commissure—and a projection system of fibres belonging to the olfactory apparatus.

In his degeneration experiments on monkeys, dogs and cats, Probst [21] found the stria to degenerate in both directions. He could trace degeneration in front into the nucleus of Ganser, and behind into the tip of the temporal lobe.

By the method of longitudinal sectioning it has not been yet possible to establish the continuity of the fibre bundles composing the stria terminalis throughout their length in the human brain. The stria is most prominent over the superior (dorsal) part of the thalamus, in the groove between it and the caudate nucleus. In that particular situation the bundles of the frontal and parietal portions of the thalamic fan abut against the thalamus in a manner that might be very misleading in sections in which large numbers of fibres are cut across. At their junction with the thalamus the lateral portions of the stout frontal and parietal bundles pass down on the lateral surface of the lateral thalamic nucleus. There they at once break up into a matted brushwork which, in these sections, produces the very characteristic appearance of the lateral aspect of the lateral thalamic nucleus—the lamina medullaris externa. The mesial portions of the bundles in question, however, do not break up into a brushwork to the same extent. As they impinge upon the thalamus, they bend either forwards or backwards, and make a mesial bulge in the dorso-lateral groove of the thalamus, where they proceed for a considerable distance before sinking into its substance (fig. 1, VIII).

The effect produced by these frontal and parietal bundles as they impinge against the dorso-lateral edge of the thalamus is the same as when a row of camel's-hair brushes is pressed against a flat surface along its edge. Those hairs which strike the surface bend in different

directions and the hairs of adjoining brushes will become intermingled; while those situated beyond the edge will pass straight down.

It is, of course, possible that mixed in among these thalamic fibres are others which pursue an arcuate course around the thalamus. It is certain, however, that the number of such fibres, if they exist in the human brain, must be very small. A number sufficiently large to form even a thin bundle could hardly fail to be detected in longitudinal sections of flattened-out tissue. It is also certain that the main bulk of the stria terminalis in man is produced not by such arcuate fibres, but by the linear bulge of the thalamic fibre-bundles as they impinge upon the lateral edge of the thalamus.

Much longer fibres than those which constitute the stria terminalis can be observed on the surface of the thalamus close to the stria. The thin superficial covering of fibres on the dorsal, posterior and inferior surfaces of the thalamus—the stratum zonale—may be peeled off with ease from the nuclear masses within. Ranson [23] has described such a long strand of tissue which he dissected away from around the thalamus, and which he called the *Fasciculus thalamo-temporalis arcuatus*. He gives, however, no account of the microscopical appearance of that strand, and its differentiation from the thalamo-temporal fasciculus described by Arnold is difficult. Serial microscopical sections cut in the longitudinal course of that band made in the present study show nowhere bundles of fibres extending from one end of the long strip to the other.

THE ORBITAL AND PREFRONTAL THALAMIC RADIATION.

The course of the fibres between the orbital and prefrontal regions of the cortex and the optic thalamus is quite unlike that of the other contingents of the thalamic radiation. From the prefrontal cortex the fibres at first curve downward and backward; from the orbital area they sweep upward and backward. Upon reaching the anterior border of the caudate nucleus, both sets of fibres curve abruptly upward, in front of and parallel to the outline of the nuclear mass for a distance of about 0.5 cm. In that situation the fibres contribute to the beginning of the subcallosal bundle. They are then gathered into thick strands which pursue a long downward and backward course through the substance of the anterior portion of the caudate nucleus, the lowest of them bending over the anterior commissure (fig. 1). In their course through

the nuclear mass the bundles divide and anastomose at frequent and irregular intervals, so that this portion of the thalamic fan has the appearance of a coarse, crude network. It is important to understand, however, that this repeated division and anastomosis of the bundles takes place not only on a sagittal plane, but in a mesial direction as well. The consequence of this is that the mesially-bulging mass of the caudate nucleus above the anterior commissure is filled by these thalamic bundles. Since the fasciculi are bent in a mesial direction, a number of them are cut obliquely in sagittal sections where they branch out from their parent bundles, at the anterior and posterior borders of the head of the caudate nucleus.

Upon reaching the anterior end of the lateral portion of the thalamus, the thick bundles break up into thinner fasciculi which pursue a parallel course for some distance and then diverge. Throughout their long course these strands show no tendency to break up into a brushwork of fibres, such as is the case to a greater or less extent with the other contingents of the thalamic bundles.

It will be remembered that the anterior surface of the thalamus bears a rough resemblance to the narrower pole of an egg, in which the anterior nucleus is wedged in between the anterior portions of the converging lateral and mesial nuclei. Below, the anterior portion of the ventral nucleus is in contact with the lateral nucleus. The sagittal sections studied are those contained in the lateral portion of the thalamus for a thickness of about 5 mm. These sections, therefore, contain but a small portion of the anterior and of the ventral nucleus—their most lateral portions.

Lewandowsky's [14] researches tend to show that the anterior nucleus of the thalamus has no direct connection with the cortex. His conclusion is corroborated by the results of the present study to the extent that the thick bundles of fibres which are found in the anterior portion of the thalamus on its lateral side traverse this region without breaking up. This author is of the opinion, too, that there exists a pathway between the anterior nucleus of the thalamus and the subthalamic body. As will be presently seen, the work of other investigators in part contradicts this opinion. It has not been possible to establish in the present study whether such a pathway exists or does not exist. The longitudinal sections, however, do point to a possible source of error in this connection. As the bundles of fibres are traced in their longitudinal course downward and backward, a number of them are seen to impinge upon the capsule of the subthalamic body. Some of

these bundles become intermingled with the dense network of the capsule and are thus lost to view; others, however, penetrate the capsule and traverse the substance of the subthalamic body for some distance. In the space between the anterior portion of the thalamus and the subthalamic body these bundles diverge; they are, therefore, more and more cut up in these sections, so that upon approaching the subthalamic body their continuation is indicated by a series of short strips (fig. 1, IX). In sagittal sections the subthalamic body appears filled with a multitude of islands of transversely cut bundles. In the midst of these, the short longitudinal strips of divided orbital and prefrontal bundles become lost. Their further course was not ascertained in the present study. Since this contingent of fibres arrives at the subthalamic body by way of the anterior portion of the thalamus, some of its most mesially lying strands might easily be mistaken for a pathway connecting the two structures.

Such a connecting pathway between the subthalamic body and the anterior nucleus of the thalamus, is to a certain extent negated by the observations of Roussy [24]. After having destroyed the greater portion of the thalamus including the anterior nucleus in a monkey, he was unable to find any trace of degeneration in the subthalamic body.

This observation of Roussy's is incompatible with the picture presented by the sections in the present study. If bundles of continuous fibres traverse both the anterior portion of the thalamus and the subthalamic body, then their destruction between those points should be followed either by direct or at least by traces of retrograde degeneration in the subthalamic body. Yet in the experiment mentioned Roussy found the latter body to be intact.

That the thalamic radiation contains both corticofugal and thalamofugal fibres, has been abundantly demonstrated by the researches of v. Monakow [17], Bechterew [2], Dejerine and Long [5], Probst [20], Roussy [24], E. Sachs [25], Fukuda [8] and a large number of other investigators. If those prefrontal and orbital bundles which traverse the subthalamic body in the human brain contain cortico-fugal fibres, then an injury to those portions of the cortex should be marked by tracts of degeneration extending into the subthalamus.

v. Monakow [17] destroyed the greater portion of the cortex in a new-born dog (Gudden's method). Six months later an examination of the brain showed the thalamus very much reduced in size on the injured side, but the subthalamic body appeared normal.

After ablation of the posterior frontal region of the dog's cortex,

Bechterew [2] found degeneration extending to the subthalamic body.

Of course, the posterior frontal region of the dog's cortex may not correspond to the prefrontal area of the human cerebrum. Yet even so, the findings in the present study are more strengthened by the positive results in Bechterew's experiment than they are weakened by the negative results in Monakow's case. The failure of development of a few strands of traversing fibres would probably cause too small a diminution in the size of the subthalamic body to be readily appreciated; while the observation of tracts of degeneration in that body after a cortical injury establishes the fact that cortical fibres either traverse or end in that body.

In the case where an old lesion involved all three frontal convolutions, Fukuda [8] found no atrophy in the subthalamic body. Whether this, too, should be discounted as a negative observation, or whether it signifies the fact that no fibres from the frontal portions of the cortex (as distinguished from the pre-frontal areas) pass into the subthalamic body, is for the present impossible to say. A concluding remark by the last mentioned author, in connection with two of his cases, throws some light on the subject. "It is not clear," he says, "where the bundles derived from the basal convolution-complex"—the prefrontal at the base, which include the orbital—"go . . . They certainly have no connection in the thalamus proper. At most they may pass to the most mesial portions, the tuber cinereum or the central grey matter of the third ventricle. . . ." This investigator, then, must have followed these bundles through the thalamus as far downward and backward as he could before he lost sight of their course.

My observations in the present study do not corroborate Roussy's [24] conclusion respecting the anterior thalamic nucleus as one of the sources of the anterior portion of thalamo-cortical fibres. Those lesions of the thalamus produced by this investigator, which involved the anterior nucleus, were large. They extended into the lateral portion of the thalamus and rather deep into its ventral and posterior portions. Fibres which may have their origin in regions behind and below the anterior nucleus would traverse it on the way to the anterior areas of the cortex. That large and numerous bundles do traverse the most lateral portion of the anterior nucleus, but which have their origin or their ending behind or below that nucleus is certain. If any of these fibres are thalamofugal, their destruction in their course through the anterior portion of the thalamus will be followed by their degeneration in a

direction toward the cortex; and the impression produced may easily be in that case that the anterior nucleus is their source of origin.

After an experimental lesion in the anterior portion of the thalamus in a monkey, E. Sachs [25] observed degenerated fibres between the anterior thalamic nucleus and the external, lateral or capsular side of the caudate nucleus. In this case, too, a possible source of error must be pointed out. The orbital and prefrontal bundles traverse the antero-lateral parts of both the thalamus and the caudate nucleus. These bundles contain a contingent of thalamofugal fibres. In a lesion of the anterior part of the thalamus, a certain number of the latter fibres must, therefore, degenerate in their course through the lateral portion of the caudate nucleus. It will be remembered that while traversing the caudate nucleus, the bundles join and divide and join again in a multitude of ways. Points of degeneration would, therefore, appear as very much scattered in this intricate network, and difficult to follow beyond it.

TRACTUS SUBTHALAMICUS.

A well-defined band of very fine fibres appears in these sections immediately beneath the subthalamic body (fig. 1, X). It lies embedded therefore, in the substantia nigra, at its highest and most lateral portion. In front the fibres become dispersed and lost in the caudoputamen, immediately beneath the anterior commissure. Posteriorly its fibres are intermingled with the temporal thalamic fibres in front of the transversely cut auditory tract. In a number of the more mesial sections the band appears to embrace and to merge with the auditory bundle. The nature of this band of fibres has not been ascertained.

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A NEW CONCEPTION OF THE ELEMENTS OF SENSATION.

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I.—INTRODUCTION.

WE owe to Head our deliverance from the chaos which existed with regard to the afferent nervous system up to the time of the publication of his reconsideration of the distribution and function of the peripheral nerves. By means of investigations by measurable tests of each form of sensation, he was able clearly to demonstrate that what had been termed "diminished sensibility" was really a state in which some forms of sensation had been lost whilst others were retained. He was able to prove conclusively that "parts which have universally been considered to be areas of diminished sensibility turn out to be totally insensitive to certain higher forms of stimulation." In the study of the recovery of cutaneous sensation after suture of a peripheral nerve, he discovered two stages. During the earlier stage there was a gradual diminution in the area insensitive to pain produced by the prick of a pin, and to heat and cold, but the recovered sensibility was appreciably altered. The prick evoked a sensation which radiated widely and caused unnatural discomfort, and although the extremes of temperature could be appreciated no sensation of heat or cold was induced by intermediate thermal degrees. During the later or second stage of recovery the affected part began to become sensitive to light touch and

to degrees of temperature which induced sensations of "warm" and "cool." With further improvement it became possible to discriminate two points applied simultaneously, and the characteristic radiation of the first stage gradually disappeared as more accurate cutaneous localization returned.

Such observations during recovery after suture of a peripheral nerve demonstrated the existence of two systems in cutaneous sensibility, which Head named the protopathic and epicritic, and it was thought that the former system regenerated more rapidly and with greater ease than the latter. The crucial test of this division into two systems was the classical experiment upon Head's own arm. In this experiment the radial nerve was divided at its origin from the musculo-spiral, and the musculo-cutaneous nerve at the point where it perforated the deep fascia, just proximal to its division into the two branches which supply respectively the anterior and posterior aspects of the pre-axial half of the forearm. Some days later it was discovered that, in addition to the larger area in which, except for the dissociation at the edges, there was a complete loss of cutaneous sensation, there existed a small triangular portion where normal sensation to light touches with cotton wool and Von Frey's hairs was retained, but there was insensitiveness to the prick of a pin. The dissociation of the sensation of this triangle was the reverse of that found at the periphery of the larger area, where the prick of a pin was appreciated but there was no appreciation of light touches with cotton wool. The prolonged investigations of these complementary areas of dissociated sensibility established the existence of the two systems in cutaneous sensibility, and proved that these two systems were independent and did not depend upon simply a modification of the same system of nerve fibres and end organs.

To these two systems found in cutaneous sensation Head added a third, deep sensibility, which was capable of responding to pressure, passive movement of joints, and pain caused by excessive pressure. He found that a part endowed with only this third form of sensibility possessed not only the ability to recognize a pressure stimulus, but also the power to localize it with remarkable accuracy. Furthermore it was decided that "the fibres subserving this form of sensation run mainly with the motor nerves, and are not destroyed by division of all the sensory nerves to the skin." Our knowledge of deep sensibility is based almost entirely upon an investigation of the residual sensation in the experiment upon Head's own arm. The nerves divided in this

experiment were selected because it was thought that, since these nerves were usually considered as purely cutaneous in distribution, a large area of skin would be rendered completely insensitive and yet the sensibility of the subcutaneous tissues would be undisturbed. Observations will be advanced in this paper to show that it is anatomically impossible to isolate deep from cutaneous sensibility, and that, by employing methods which Head has used for the investigations of cutaneous sensation, it is possible to find after division of peripheral nerves at various levels most intricate types of dissociation in the various forms of sensibility grouped as "deep." Furthermore, having obtained an insight into the production of these dissociations, it is practicable during regeneration after suture to recognize two systems in deep sensibility.

My attention was directed to this subject during the progress of a study of the late results of secondary suture of certain peripheral nerves of the upper limb [7]—as the median and ulnar—since it became apparent that the sensory condition found did not conform with our present conception of the subject. The chief discrepancy had reference to deep sensibility, and most of the investigations recorded in this paper are concerned with this aspect of sensation. It was discovered in some patients, after suture of the median, that all the muscles—when tested individually—had recovered voluntary power and yet the hand was of slight practical service when the patient attempted purposive movements necessary on his return to work. These patients complained that they lost the grip of their tools, and on further inquiry it was found that they could use the hand fairly well as long as they concentrated upon the movements, but it failed to function satisfactorily as soon as they ceased to watch what it was doing. Several volunteered the information that the hand was useless in the dark or when they were unable to observe what they were trying to do with it. Such complaints were made by patients some three or more years after the performance of end to end suture, even when the cutaneous sensation had made a fair recovery and all the muscles, when tested individually, exhibited good voluntary power. It seemed clear that such a disability could only be due to a loss of afferent stimuli from joints, muscles, tendons and other deep structures. It was only practicable to investigate directly the extent of the recovery of fibres conveying sensory impressions from such deep structures as the joints. An investigation as to the sense of posture and the appreciation of passive movements in the finger and thumb articulations supplied by the nerve was carried

out and it was discovered that these were generally lost, or at the best very defective, even when fully three years had elapsed since the time of the suture. This loss of appreciation, or defective recognition, of passive movement in the joints supplied by the nerves was found irrespective of the level of the suture; although, according to Head, there would be no serious loss of deep sensibility after section of the median or ulnar nerves low down, e.g., at the wrist. This inquiry into the recovery after end to end suture of afferent fibres from joints gradually directed me to the investigations recorded in this paper.

II.—THE ANATOMY OF DEEP SENSIBILITY.

By the subdivision of sensation into cutaneous (epicritic and protopathic) and deep, we are at once confronted with certain anatomical difficulties, which are emphasized in the hand and digits where much of the experimental work upon sensation has been performed. We cannot separate anatomically the fibres distributed to cutaneous and subcutaneous structures of any sensory nerve of sufficient size to warrant its use as a source of information about sensation. No nerve trunk or branch, of sufficient size to receive a name, has an exclusively cutaneous distribution. My own clinical investigations prove that the radial [8], besides supplying skin is distributed to certain articular structures, and careful dissection of nerves which have unfortunately been described as "purely cutaneous" will show that a large proportion of fibres terminate in the subcutaneous tissues. Of course such a gross method of investigation as dissection does not give us any information about the function of these fibres which can be traced into deeper structures, but in view of the clinical findings after division of the radial nerve (which is usually designated a purely cutaneous nerve), we must not assume that any nerve, of sufficient size to justify its selection for experimental work upon sensation, is purely cutaneous until it has been proved. In the course of this work the extreme difficulty of determining clinically whether the sensory fibres of a nerve are distributed solely to skin or not has become manifest, the chief hindrance arising from the fact that we cannot ascertain for certain whether some aspects of sensation are subserved by fibres terminating in skin, or subcutaneous tissues, or both. This difficulty is well illustrated by localization. From the experiments upon localization it is clear that fibres subserving this form of sensibility terminate cutaneously and subcutaneously. It seems possible from my own observations and those of others that discrimination may be also served by both cutaneous and subcutaneous systems,

but there are even greater technical difficulties to be overcome in making a decision with regard to this form of sensation. At first sight the experiment upon Head's own arm seems to establish discrimination as purely dependent upon a cutaneous supply, but it depends upon the *assumption* that the radial and the terminal branches of the musculo-cutaneous are purely cutaneous nerves, and since in a larger proportion I have found this not to be the case, the results cannot be accepted as proof that discrimination is only a cutaneous form of sensation. In the case of division of the median and ulnar it is clearly quite impossible to advance any proof with regard to this question owing to the complex anatomical distribution to subcutaneous tissues in this region. Whereas we know accurately the normal cutaneous distribution of the median and certain variations [6] in its cutaneous supply, we find that the corresponding deeper tissues receive sensory fibres from at least three sources. The subcutaneous structures of the palmar surface of the thumb, index and middle fingers are supplied from the median nerve direct by means of the digital branches, and from branches arising from the main trunk proximal to the wrist which probably run chiefly with the muscular branches, and so pass to their distribution along tendons. The subcutaneous tissues of the palm corresponding to the cutaneous distribution of the median are supplied, first by branches from the nerve itself as it breaks up in the palm, secondly by branches which pass down with the long tendons, and thirdly from the deep branch of the ulnar or perforating branches of the radial or both. The latter two possible sources of sensory fibres are shown by the fact that even after division of the median nerve in the upper arm, pressure and often pressure-pain can be recognized over the whole of the palm in some patients, and in all over a considerable part of the palm; and similarly after division of both the median and the ulnar in the arm contact and pressure pain are appreciated over part of the palm, especially on the outer side.

The distribution to subcutaneous tissues in the case of the ulnar is not quite so complex, but sufficiently intricate to make it impracticable to isolate it from the cutaneous supply. In the hand deep sensibility is only in part subserved by fibres which run with muscular branches, since the digital nerves—which are generally regarded as cutaneous—definitely supply the articulations [8]. One form of sensation included under the term of deep sensibility is therefore invariably affected by division of the median or ulnar, whether the section of the nerve occurs at the wrist or in a more proximal part of the limb.

The complex anatomical arrangement of the sensory supply to the subcutaneous tissues of the hand makes it exceedingly difficult to investigate what has been termed deep sensibility; it is not accurate to regard it as the residual sensation after division of a purely cutaneous nerve unless we are certain that a nerve so designated has solely a sensory distribution to skin, and from the results recorded in this paper I maintain that we cannot so adjudge the radial nerve. Most anatomical text-books describe the radial as "purely" or "solely" cutaneous, but it seems evident that in the past anatomists have designated nerves as purely cutaneous on insufficient evidence. This appears to have misled Head and his co-workers into the belief that in "a human experiment in nerve division" only cutaneous sensation was destroyed, and deep sensibility persisted undisturbed.

From these conclusions it would appear that any division of sensation into cutaneous and deep must be regarded as artificial, and is apt to be misleading when applied to clinical work owing to the complex anatomical distribution of sensory fibres to the subcutaneous tissues.

III.—THE NORMAL ANATOMICAL DISTRIBUTION OF AFFERENT NERVES TO THE INTERPHALANGEAL AND METACARPO-PHALANGEAL JOINTS.

After a few patients had been examined with reference to the extent of the recovery of sensory fibres supplying the articulations of the digits, a difficulty presented itself owing to our imperfect knowledge of the normal distribution of peripheral nerves to the interphalangeal and metacarpo-phalangeal joints. Consequently it became necessary to discover precisely the normal distribution of the various nerve trunks to the joints, in order to be able to estimate accurately the recovery which had occurred. The details of this part of the work have already been fully recorded in a recent paper [8] and it is necessary only to summarize the conclusions bearing upon deep sensibility.

In all fifty-one patients were examined and they were selected because it was known that a complete division of definite peripheral nerves of the upper extremity existed. Any patient manifesting such complications as division of tendons or limitation of mobility of joints was disregarded for obvious reasons.

The examination was first made on the normal side in order to make the patient quite familiar with the method and what was expected of him; secondly to provide a standard and control for comparison;

and thirdly to enable me to test the reliability and attention of the patient. It was surprising how few patients had to be discarded as unreliable when sufficient time was taken to make quite clear to them what was wanted, and enough patience was expended. A relatively large number, who were otherwise suitable, had to be omitted on account of arthritic adhesions. Each segment of the digit, above and below the joint to be examined, was grasped firmly by the lateral borders and then the joint was gradually and evenly flexed or extended. The segments of the digit must be grasped firmly, as Head [3] has pointed out, so that the additional pressure required to move the joint shall not be distinguishable and thus lead to the recognition of movement from impressions other than those arising from the articular structures. The movement of the joint must also be made as far as possible at a uniform rate and not too slowly. The patient was requested to state when he first felt any movement, and on answering was further asked at which joint it occurred, and also the apparent direction of the movement. The latter two questions were soon found to be of fundamental importance for any accurate investigation of the appreciation of passive movement in a *joint*, since it was discovered that patients were able frequently to recognize movement of a particular digit without possessing any knowledge of the joint at which it occurred or the direction in which it moved. Quite early in the investigation it became manifest that this recognition of mere movement of a finger was obviously dependent upon alteration in tension or position of the tendons (and consequent stimulation of the nerve endings in relation to them), and did not arise from any stimulation of afferent terminals in the bones, cartilage, and capsule of the joint. Several patients informed me that they felt the movement of something at the wrist and knew it was pulling on a finger, but were quite unable to discover from the sensation aroused at which joint the movement took place. Fortunately this source of fallacy was discovered at an early stage in the investigation, and errors arising from it were consequently prevented. From a review of other work on this aspect of sensation it seems possible that fallacies may have arisen in the past from this cause.

Another source of possible error, which was soon determined, arose from the difficulty patients had in expressing the joint at which the movement was experienced. Such a term as "first joint" was apt to be misleading, since some referred this to the metacarpo-phalangeal articulation, and others to the distal interphalangeal. Consequently it was found necessary at the outset of each examination to have a clear

TABLE I.—TO SHOW THE NORMAL VARIATION IN THE DISTRIBUTION OF AFFERENT NERVES TO THE INTERPHALANGEAL AND METACARPO-PHALANGEAL JOINTS.

Thumb		Index			Medius			Ring			Little	
Interphal.	Met-phal.	Distal interphal.	Prox. interphal.	Met-phal.	Distal interphal.	Prox. interphal.	Met-phal.	Distal interphal.	Prox. interphal.	Met-phal.	Distal interphal.	Met-phal.
(1) Median chiefly supplementary (1) Radial chiefly supplementary	(1) Radial chiefly supplementary (1) Median supplementary	Median (invariably)	Median (invariably)	(1) Median chiefly supplementary (1) Radial supplementary	Median (invariably)	Median (invariably)	(1) Median chiefly supplementary (1) Radial supplementary	(1) Ulnar (Probably supplemented by median)	(1) Ulnar (1) Ulnar (1) Ulnar	(1) Ulnar	Ulnar (invariably)	Ulnar
(2) Median alone 42 per cent.	(2) Radial alone 15 per cent.			(2) Median alone 25 per cent.			(2) Median alone 42 per cent.	(2) Ulnar alone 25 per cent.	(2) Ulnar alone 25 per cent.	(2) Ulnar alone 5 per cent.		
	(3) Median alone 16 per cent.			(3) Radial alone 8 per cent.			(3) Radial alone 8 per cent.			(3) Very rarely branches from radial		
				(4) Very rarely some branches from ulnar			(4) Barely some branches from ulnar					

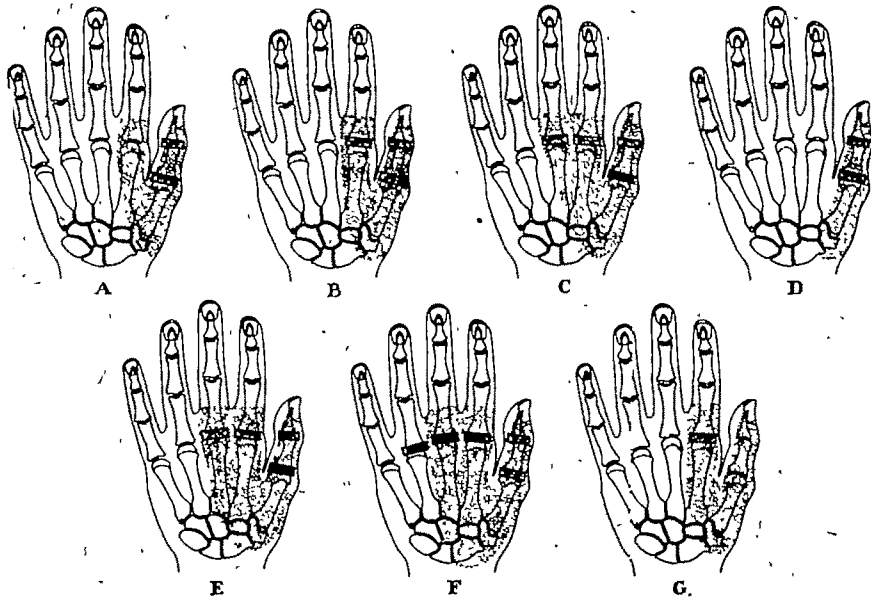
understanding with the patient as to the terminology he adopted for the various joints. The results of this anatomical inquiry into the normal supply of the afferent fibres to the interphalangeal and metacarpophalangeal joints are summarized in Table I, but it must be understood that the percentages there stated can be regarded as only approximate, since only fifty-one patients were examined.

The most surprising result found in these examinations was that no difference in the extent of the loss of the recognition of posture and appreciation of passive movement was produced by section of the nerve under inquiry at different levels in the limb, a precisely similar distribution being found whether the nerve was severed in the upper arm, forearm, or at the wrist. In seven patients (median four, ulnar two, median and ulnar one), the division was at the wrist, and there had been no division of tendons, yet the loss of appreciation of passive movement was just as widespread and as profound as when the nerves had been divided in the upper part of the forearm. In twenty others the division had occurred in the forearm, and in a number of these in its distal part. The patients in the latter category did not manifest any loss of the recognition of pressure, yet the loss of appreciation of posture was just as extensive as after section in a more proximal part of the limb, even where one or more digits were completely anaesthetic to all forms of stimulation.

It is of particular importance to notice the condition found in fourteen patients in which the musculo-spiral had been severed, since the study of these patients really resolved itself into an investigation of the distribution of the radial and lower external cutaneous branches of this nerve to the joints. In two the recognition of passive movements appeared to be perfect in all the joints, but in the other twelve one or more articulations of the thumb or fingers were affected, and the extent of this distribution was found to be subject to considerable variation. It will be remembered that there was no disturbance of the perception of passive movement in Head's historical experiment upon which depends our present knowledge of deep sensibility; and it seems possible, from the fact that a similar result was found in only two patients out of fourteen, that this form of distribution is the exception rather than the rule. Furthermore in view of the evidence of the very frequent presence of sensory fibres in the radial for the supply of certain articulations of the digits, it is no longer possible to regard the radial as a purely cutaneous nerve.

In the course of this study a very intimate relationship between

the variations in the cutaneous (epicritic) and articular distributions of the various nerves was observed, and this is illustrated in fig. 1:—



■ = Complete loss of appreciation of passive movement.
 ■ = Impaired recognition of passive movement.
 . = Extent of anæsthesia to lightest possible stimulations.

Type A = 1 patient.
 „ B = 4 patients.
 „ C = 3 patients.
 „ D = 1 patient.

Type B = 1 patient.
 „ F = 1 patient.
 „ G = 1 patient.

FIG. 1.—To show the intimate relationship between the cutaneous (epicritic) and articular distributions of the radial nerve.

The loss of the appreciation of passive movement in the joints of the digits which exhibit no anæsthesia to tactile pressure is at first sight rather mystifying in view of our present conception of the pathway for the deep afferent impressions, i.e., along nerve-fibres which run chiefly with muscular branches and so reach the articulations by the way of such channels as tendons and blood-vessels. This view must largely disregard the digital branches of such nerves as the median and ulnar as a source of articular branches to the interphalangeal and metacarpo-phalangeal joints, and yet a simple dissection of these branches will demonstrate clearly fine filaments which pass to the periosteum of the phalanges and to the interphalangeal articulations. It may be presumed that these branches from the digital nerves are either afferent or vasomotor in function. The results found in the

clinical examinations just recorded of patients suffering from division of the median or ulnar at the wrist, uncomplicated by any injury to the tendons, appear to show conclusively that some of these filaments are afferent in function and transmit information which enables us to appreciate the site, direction, and range of passive movement. Since the extent of the loss of appreciation of passive movement was not altered by the anatomical level of the section of the nerve, it appears that few, if any, fibres subserving this form of deep sensibility run with the branches to forearm muscles, the tendons of which are inserted into the phalanges. Several patients suffering from division of the median or ulnar at the wrist were able to recognize "movement" of a particular finger, probably as a result of alteration of tension or position of the long tendons; but it was clear that this knowledge was not produced by stimulation of afferent terminals in the neighbourhood of the joint, since some of them explained that they felt "the pull at the wrist," and so "guessed a finger was being moved." None of these were able to recognize at which joint the movement occurred, or in what direction it was made.

These conclusions have been verified upon a number of patients examined three or more years after suture of the median or ulnar nerve at the wrist, who at the best still exhibited very defective recovery of the appreciation of passive movement in the joints supplied by the affected nerve. From these investigations it appears that the digital nerves are the only important source to the joints of branches which transmit impulses that enable us to recognize position and movement.

On applying this knowledge to the examination of large numbers of patients upon whom end to end suture of the median, ulnar, or musculo-spiral nerves had been performed, it was found that this form of sensation, irrespective of the level of the suture, failed to show any signs of recovery until a very late stage—a time when there was evidence of return of epicritic sensibility.

IV.—LOCALIZATION.

The findings with regard to spacial recognition in three dimensions led me to investigate other aspects of deep sensibility.

At present it is believed that pressure is localized with remarkable accuracy even when there is a complete loss of cutaneous sensibility, and it is surmised that this form of sensation is dependent upon

afferent fibres which run in muscular, articular, and subcutaneous branches.

Hitherto, no perfectly satisfactory method for testing accurately tactile localization has been evolved. Most methods now in use only demonstrate very gross defects, and fail to furnish measurable results. The tests most frequently adopted in the investigation of tactile localization only show such a gross error as failure to recognize correctly the segment of the digit upon which the pressure has been applied—a defect which I have found to occur several times in apparently normal individuals [9]. Consequently an effort was made to discover some method which would supply more accurate information about the power of localization, and also provide measurable results. The method found to be most serviceable and practicable was a slight modification of that described as Henri's, but, unfortunately, it has not been possible for me to procure the original description of his method. The patient, having the part to be tested obscured from his vision, marked upon a life-sized diagram the position of the point judged to be stimulated, whilst the observer recorded on another similar diagram the exact point touched. After a sufficient number of points had been localized, the two diagrams were superimposed and the two points recorded in each test were marked on one diagram—in different colours or by distinctive signs, and then the error in each case was measured off with a millimetre scale. From these measurements, if a sufficient number of points had been localized, the average error for the whole or individual parts—as each digit—could be determined. In the latter part of the investigation only one chart was used, the observer recording the exact point stimulated after the person examined had marked the point where he felt the stimulation; and this simpler procedure proved as successful, and apparently as reliable, as the more tedious original form.

Using this method, which possesses the great advantage of giving measurable results, the following experiments were performed:—

Experiment 1.—This series, in which ten members of the medical profession provided the subjects for examination, was undertaken at the outset for two principal reasons. In the first place it was thought that any possible fallacy due to unfamiliarity with the diagrams would be reduced to a minimum; and, secondly, such a series would provide valuable information with regard to the introspective aspect of this form of sensation. The tactile pressure was made by a blunt instrument about 0·2 cm. in diameter. The palmar and dorsal surfaces of

each hand and digit were explored in turn. Twelve stimulations were made on each surface, eight or nine of which were on the digits and the rest on the palm or dorsum of the hand. The average error for the ten subjects was found to be 0.6 cm. for the palmar and 0.5 cm. for the dorsal surfaces of the right hand and fingers, and 0.5 cm. for both surfaces of the left hand and fingers.

Experiment 2.—In this series, ten non-medical people were examined and only the palmar surface of the two hands and digits explored. The ten were composed of clerks, departmental stewards, porters, and second-year students. The same number of stimulations were made, and the same proportion on the hand and digits, by the same instrument as in the previous experiment. The average error for the ten was 0.6 cm. for the right hand and 0.7 cm. for the left. The close similarity in the results in the two experiments is rather remarkable, and shows that any error due to unfamiliarity with the charts, at any rate for the palmar surface of the hand and digits, must be very slight. This conclusion was confirmed by a large series of tests carried out upon pensioners under my charge, in whom an average error of 0.6 cm. was found for the palmar surface of the hand and digits on both sides.

Experiment 3.—This series was undertaken to discover the normal average error for the individual fingers and to find out if there was normally any definite variation in the power of localization in the different fingers. Two people were chosen from each of the former experiments and twelve pressure stimulations (six on the palmar and six on the dorsal surface) were made on each finger of right hand. As far as possible two stimulations were made on both surfaces of each segment of a finger.

The average error for the four persons examined was found to be 0.4 cm. for the index, middle, and ring fingers, and 0.3 cm. for the little finger; from which it appeared that the power of localization did not vary to any obvious extent in the four fingers.

Further details and tables showing individual errors in these three experiments are given in the paper previously referred to.

Experiment 4.—From the results which were being found on applying this test to patients suffering from division of peripheral nerves, it was decided to perform a series of tests using as a stimulus a hair, which could not possibly stimulate any but cutaneous nerve terminals. For this investigation three medical people were chosen from those used in Experiment 1 and a similar number from the non-medical group of

Experiment 2. The same number of stimulations were made with the hair as in the former experiments where pressure had been used as the stimulus, and the conditions under which the tests were performed were identical with those of the previous experiments. It was found that a purely cutaneous stimulus could be localized very accurately; in Table II the results are compared when using a hair and when using pressure with an instrument 0.2 cm. in diameter. The latter records had been taken some weeks previously.

TABLE II.

	Right Hand			Left Hand	
	Hair	Pressure		Hair	Pressure
SL.	.5 cm.	.4 cm.	..	.7 cm.	.6 cm.
SJ.	.5 "	.7 "	..	.7 "	.5 "
EAL.	.6 "	1.0 "	..	.5 "	.8 "
AFCD.	.5 "	.5 "	..	.4 "	.6 "
AG.	.6 "	.7 "	..	.7 "	.7 "
RF.	.5 "	.5 "	..	.5 "	.5 "
Average	.5 "	.6 "	..	.6 "	.6 "

From these results it will be seen that accuracy of localization is practically the same, for either a purely cutaneous stimulus or pressure, in individuals with normal sensation.

It is of interest to notice that in the observations made upon Head's hand [5], it was found that accurate localization of cutaneous stimuli did not return until the skin was sensitive to tactile hairs after shaving.

Experiment 5.—After the former more or less preliminary experiments, which were undertaken chiefly to gain experience and establish the normal degree of error in localization, had been carried out, the pressure test was applied to twenty patients who were known from surgical observations to have suffered from division of one or two peripheral nerves of the upper limb at various levels. A similar number of stimulations as in Experiments 1 and 2 were made over the region of the cutaneous distribution of the affected nerve and, for comparison, on the normal part of the same hand or a similar region on the unaffected hand. Stimulations were made with the same instrument as that used in the other experiments. In ten patients, the observations were taken shortly after the performance of secondary suture of the injured nerve, at a time too early for any regeneration to have occurred. The results are tabulated in Table III.

The average error for the ten patients over the cutaneous field of the sutured nerve was 1.4 cm., whereas on the normal part it was 0.6 cm.

TABLE III.—LOCALIZATION (PRESSURE) TESTS, AFTER COMPLETE NERVE DIVISION AND SUTURE AT A TIME WHEN NO REGENERATION HAD OCCURRED.

Patient	Nerve	Site of suture	Average error for localization over area of epicritic loss	Average error for localization over normal area
T. E.	Median	Upper forearm	1.2	.6
J. D.	Median	Middle of forearm	1.4	.5
H. S.	Musculo-spiral	Elbow	1.1	.4
T. M.	Ulnar	Middle of forearm	1.7	.7
A. M.	Median	Middle of forearm	1.0	.5
N. D.	Ulnar	Middle of forearm	1.2	.4
J. J. T.	Median	Arm	1.8	.6
A. L. B.	Ulnar	Elbow	1.1	.6
J. T. S.	Ulnar	Lower forearm	1.9]	.8
F. S.	Ulnar	Middle of forearm	1.2	.8

In the case of T. M. two stimulations on the little finger had to be left out of the calculations since he said he was unable to place them; he knew one was "somewhere" on the little finger, but the other seemed "somewhere" on the inner part of the hand.

In seven other patients the investigation of localization was made after protopathic sensibility had made a complete recovery, but before there was any reduction in the loss of epicritic sensibility. The results of this set are recorded in Table IV.

TABLE IV.—LOCALIZATION (PRESSURE) TEST, AFTER COMPLETE NERVE DIVISION AND SUTURE, WITH RECOVERY OF PROTOPATHIC SENSIBILITY AT TIME OF OBSERVATION.

Patient	Nerve	Site of suture	Average error for localization over area of epicritic loss	Average error for localization over normal area
B. K.	Median and ulnar	Wrist	1.4	.9
A. N. K.	Ulnar	Elbow	1.4	.5
S. O.	Ulnar	Middle of forearm	1.4	.5
J. R. M.	Ulnar	Upper forearm	1.6	.5
O. R.	Median	Middle of forearm	1.4	.8
V. P.	Ulnar	Lower forearm	3.0	.5
T. T. P.	Median	Lower forearm	1.1	.5

The average error for the seven patients over the area of epicritic loss was 1.6 cm. and over the normal part 0.6 cm. This series shows that the error in localization is not diminished during the recovery of protopathic sensibility. In two additional patients considerable time had elapsed since the performance of the suture and some recovery of epicritic sensibility had occurred, as well as the return of protopathic sensibility. In both patients gross errors were found with the compass test over the cutaneous distribution of the nerve, although this was sensitive to the lightest application of a camel hair-brush. The findings of these two patients are shown in Table V.

It is of great interest to notice that in both patients the remaining

deficiency in sensation affected discrimination, localization, and the recognition of posture and passive movement in the joints supplied by the nerve.

TABLE V.—LOCALIZATION (PRESSURE) TEST, AFTER COMPLETE NERVE DIVISION AND SUTURE, WITH RECOVERY OF PROTOPATHIC AND PARTIAL RECOVERY OF EPICRITIC SENSIBILITY AT TIME OF OBSERVATION.

Patient	Nerve	Site of suture	Average error for localization over area of partial epicritic loss	Average error for localization over normal area
W. H.	Ulnar	Arm	1.0	.7
T. N. W.	Median	Upper forearm	1.3	.9

In one other patient the only evidence of any regeneration of afferent fibres was a slight recession of protopathic loss, although four years had elapsed since the time of the secondary suture of the median, and the error in localization for the anæsthetic area was 1.2 cm., whereas for the normal part it was 0.4 cm.

By the application of this method of testing localization, which gives measurable results, to patients known to be suffering from division of peripheral nerves, it is shown that, contrary to the present view, accurate tactile localization is not present even when the pressure is sufficient to stimulate the deep afferent system. It is difficult to decide whether the defective power of localization in these twenty patients was due to loss of cutaneous or subcutaneous nerve terminals, or both, since pressure may stimulate both, and although in eighteen of the patients the skin was anæsthetic, we have no accurate anatomical or physiological information about the fibres of the median or ulnar distributed to subcutaneous tissues.

Experiment 6.—Head [5] has stated that "localization is in all probability the sum of two sets of sensation, one of which arises from deep, the other from cutaneous stimulation." The foregoing experiments are in perfect agreement with this contention, but it is difficult to decide whether the errors in localization in Experiment 5 were due to the loss of cutaneous sensation only, or to a disturbance of the deep system in addition. The power of localization which remains, in the patients used in Experiment 5, must be entirely dependent upon the deep system, but for the anatomical reasons stated in an earlier section, we cannot claim that it represents the normal power of localization served by fibres terminating in subcutaneous tissues. In an endeavour to arrive more closely at a correct conception of the part played by the cutaneous and deep systems, several preparations were applied to the unbroken skin in an attempt to obtain an uncomplicated cutaneous

anæsthesia. None of these gave a satisfactory anæsthesia, until on the suggestion of my colleague, Professor R. B. Wild, a 10 per cent. solution of cocaine hydrochloride in chloroform was used. With this it was generally found practicable to get an almost complete cutaneous anæsthesia of a small area in about ten to fifteen minutes. The solution was applied to the dorsum of the left index finger in three of the subjects used in Experiment 3. When the skin was found, by testing with a wisp of cotton wool, to be satisfactorily anæsthetized the examination of localization was made by eight pressure stimulations. At a later date the normal power of localization of the same part was tested by eight pressure stimulations. The average error for the eight stimulations, in the three subjects with and without cutaneous anæsthesia, are shown in Table VI.

TABLE VI.

		Normal average error		Average error with cutaneous anæsthesia
S. L.	..	.3 cm.	..	.4 cm
A. F. O. D.	..	.2 "	..	.2 "
S. J.	..	.2 "	..	.3 "

It will be seen that in the three subjects the power of localization was almost as accurate when there was cutaneous anæsthesia as normally. It is only possible to anæsthetize satisfactorily a small cutaneous area and this may be raised as a criticism, but although only the dorsum of one finger was examined the result of the experiment strongly favours the presumptions that:—

- (1) Accurate localization is possible through the deep system alone.
- (2) Since the errors in localization in the twenty patients examined in Experiment 5 were gross, there was a disturbance of localization through the deep system and the errors were not dependent upon a loss of cutaneous localization.

In several of the patients examined in Experiment 5 the division of the nerve occurred at the wrist or in the lower part of the forearm, and there was an average error of twice the normal. Therefore we may suggest with some confidence that accurate localization through the deep system alone is disturbed by a section of the median or ulnar at the wrist.

V.—PRESSURE PAIN.

To investigate deep sensibility further it was necessary to test that form of sensation which is now well known as pressure pain.

For this purpose an algometer was made for me similar to that used

by Rivers [3]. From some preliminary tests with the instrument it became clear that certain technical difficulties in its use were to be overcome, and it appeared necessary to carry out at the outset some experiments upon normal individuals in order to establish a standard procedure when using the instrument upon patients.

Experiment 1.—These preliminary tests were made upon six normal individuals, three on the right hand and three on the left, and in each the pressure was applied at eight selected points which are shown in fig. 2. At each point three readings were taken, and it was soon found

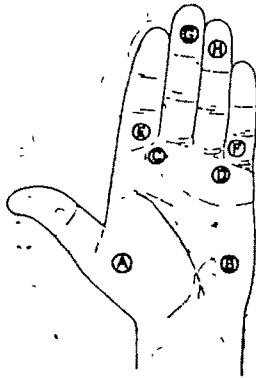


FIG. 2.—To show the position of the eight selected points used in Experiment 1 (pressure pain).

that the second and third readings ought not to be taken over the exact point of the former, since repetition of pressure over the same spot resulted in pain being experienced with much less pressure than on the previous occasion. Inequality in the three records in the same neighbourhood was found to be due to differences in the rate of application of the pressure; it was therefore necessary to apply the pressure evenly and slowly, which is by no means easy, and some of the greater differences in the three readings may be due to this cause. A third cause of difficulty was due to the personal factor, as it was not always possible to get the person examined to indicate at once the onset of the painful element in the sensation aroused by pressure. In the first series, several informed me that there was a great tendency to compare a second experience of pain with the first, which tended to disturb their judgment. These sources of fallacy make it important, as Head has already stated, to take at least three readings at each point.

The results of the investigation of the six normal individuals are given in the Table VII, which shows all the three readings at each of the eight points.

TABLE VII.—TO SHOW THE AMOUNT OF PRESSURE REQUIRED TO INDUCE PAIN, AT EIGHT SELECTED POINTS ON THE HAND AND DIGITS, IN SIX NORMAL INDIVIDUALS.

	A	B	C	D	E	F	G	H
S. J.	2.50	3.25	1.50	1.25	3.00	2.50	1.00	.75
	2.75	3.00	1.25	1.25	2.00	2.50	.75	.75
	2.50	3.50	1.25	1.50	2.50	2.50	1.25	1.00
G. M. D.	2.50	2.50	1.50	.50	2.25	2.00	.50	.25
	2.00	2.25	1.25	.50	1.00	1.50	.75	.25
	1.75	1.75	2.00	.75	1.25	1.75	.25	.25
D. S.	2.75	2.00	1.25	1.00	1.00	1.00	.25	.5
	2.00	2.50	1.00	.75	1.25	.75	.25	.75
	1.00	2.50	.75	.75	1.50	.75	.25	.25
R. F.	2.25	2.25	1.25	1.00	1.75	2.00	2.00	1.75
	2.25	1.00	1.50	1.25	1.75	1.50	2.25	.50
	1.75	1.75	1.00	1.00	1.50	1.25	1.75	1.25
L. S.	1.50	2.00	.75	1.00	1.25	.75	.50	.25
	1.75	2.00	.75	.50	1.50	1.50	.50	.25
	1.75	1.50	.75	1.00	.75	1.25	.25	.50
H. G.	2.75	3.50	1.50	2.25	2.75	2.50	2.25	2.25
	2.50	3.00	1.50	2.25	2.50	2.75	2.00	2.25
	2.75	3.25	2.25	2.75	2.75	2.75	2.00	2.25

The results of this experiment brought out the following information:—

(1) Greater pressure was usually required to produce pain in the thenar and hypothenar regions than at the other points tested.

(2) Less pressure was required at the base of the clefts between the fingers than over the palmar surface of the proximal segment of the digits. This is presumably due to the exposed position of the digital nerves as they divide in the region of the clefts into branches for the adjacent sides of the neighbouring fingers.

(3) With a single exception, less pressure was needed to induce pain over the palmar surface of the distal segment of a digit than over its proximal segment.

Experiment 2.—With the knowledge and experience gained from this preliminary investigation of pressure pain, the test was applied to a number of patients suffering from division of the median or ulnar nerves. To simplify the presentation of the results of this experiment only the average of the three readings at each point is recorded, and for ease of comparison the results of five typical tests are represented in a diagrammatic form (figs. 3, 4 and 5). As in the former experiment the pressure required to induce pain is recorded in kilogrammes.

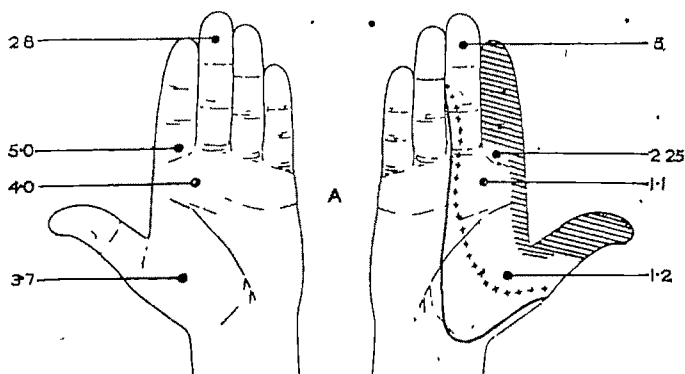


FIG. 3, A.—Division of median nerve in arm

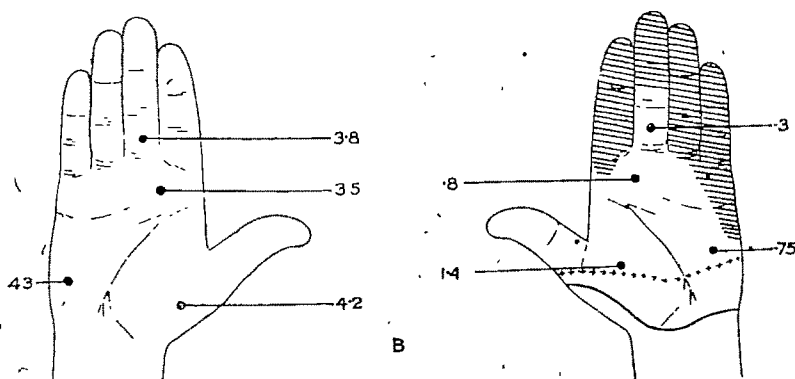


FIG. 3, B.—Division of median and ulnar nerves in arm.

Crosses = analgesia to prick of pin.

Thick line = anaesthesia to lightest applications of fine brush.

Shading = complete sensory loss.

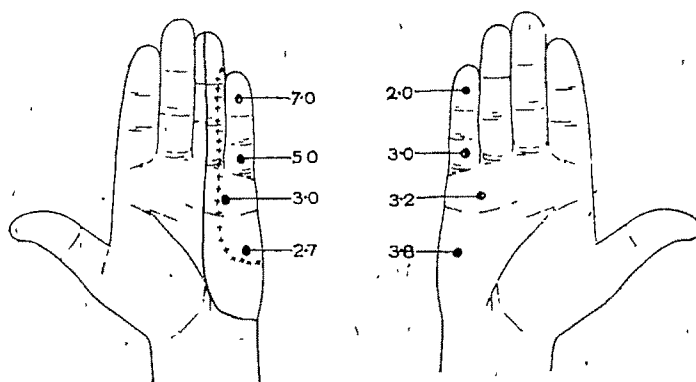


FIG. 4.—Division of ulnar nerve in upper forearm.

Crosses = analgesia to prick of pin.

Thick line = anaesthesia to lightest applications of fine brush.

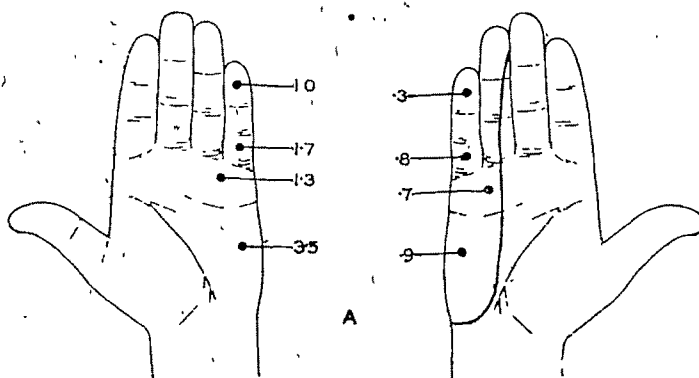


FIG. 5, A.—Division of ulnar nerve in lower forearm.
Thick line indicates anæsthesia to lightest applications of fine brush.

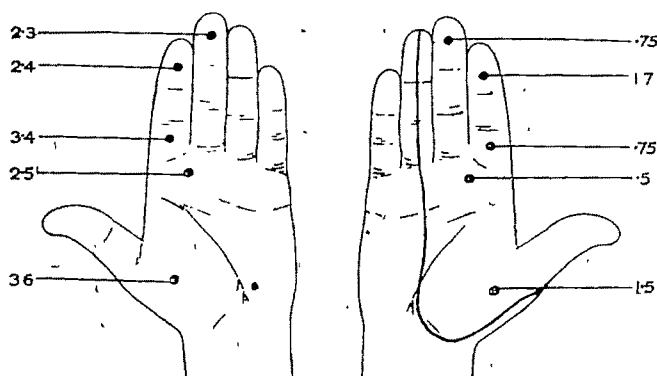


FIG. 5, B.—Division of median nerve in arm.
Thick line indicates anæsthesia to lightest applications of fine brush.

By these experiments it was found :—

(1) That it was distinctly easier to test pressure pain on the abnormal than on the sound side. This was due to the fact that when testing over an area where epicritic sensibility was lost, the patients could more readily recognize the onset of the painful element since it commenced abruptly and rapidly became intensely painful. Several patients told me that they had no doubt on the affected side, whereas on the sound side they were often in difficulty as to when the pressure became actually painful. As Head found, several expressed fear at the application of pressure on the affected side, and this, together with the

experience that on this side the pain quickly became intense, may have caused, in some of the tests an abnormally low reading on the affected side.

(2) In those patients where the division of the nerve was in the distal part of the limb and there was no absolute sensory loss, the readings on the affected side tended to be definitely lower than on the sound side.

(3) In some patients with division of the median in the middle of the forearm, i.e., proximal to the supply of that portion of the flexor sublimis digitorum which flexes the index finger and distal to the origin of the anterior interosseous nerve and branches for the supply of the main flexor mass, considerably more pressure was required on the index on the affected than on the sound side. These results pointed to a disturbance, but not complete loss, of this form of sensation in the index after division of the median proximal to the origin of the most distal branch to the flexor sublimis digitorum, and indicated that some fibres for this form of sensation in the index were transmitted by this muscular branch, and probably extended to the digit along the tendon. Similarly, after division of the ulnar in the upper part of the forearm, although the inner part of the flexor profundus digitorum was capable of voluntary action, higher readings were sometimes found on the little finger on the affected side than on the sound side. It is not so easy to give an anatomical reason for this occurrence, which is found only in a proportion of cases of division of the ulnar in the forearm and is nothing like so constant as the similar condition just described in the case of the median, but it may be due to the occasional appearance of an extra branch to the flexor profundus digitorum in the lower part of the forearm.

The associated demonstrable disturbance of the appreciation of contact in these cases will be referred to in the next section.

(4) In the patients examined during recovery, when there was a complete return of protopathic sensibility (fig. 5), the readings at all points on the affected side were lower than on the normal side. This was found even over digits that at the outset had exhibited an absolute sensory loss, or which originally had given a higher reading. These results indicate that the recognition of pressure pain returns at an early stage in recovery, at the same time as protopathic sensibility. It is also significant that in cases of only partial recovery of sensation pressure pain like protopathic sensibility is one of the most constant to manifest some improvement.

VI.—RECOGNITION OF THE "CONTACT" OF TACTILE PRESSURE.

In routine examinations of patients suffering from injury to, or disease of, the peripheral nerves, this aspect of deep sensibility is usually the only one tested. Consequently if the patient appreciates everywhere the contact of some instrument, as the head of a pin, "no loss of deep sensibility" is generally recorded in the notes. It does not seem to have been realized previously that the various forms of sensation grouped together as deep sensibility may be dissociated, and this, together with the widespread belief that deep sensibility is practically entirely transmitted by afferent fibres which run with motor nerves and reach their termination by accompanying such structures as long tendons, has been responsible for the confidence with which observers have been content to investigate simply the recognition of contact as the standard test for deep sensibility.

As is to be expected this form of deep sensibility is only appreciably affected in lesions in the proximal part of the limb, i.e., above the origin of the supply of branches to the long flexors of the digits. There is no doubt that mere recognition of contact is chiefly transmitted by afferent fibres which run in the branches to the long flexor muscles of the digits. In this respect it is instructive to refer to the fairly constant occurrence of complete anæsthesia of the distal part, and sometimes the whole of the palmar surface of the index finger after complete division of the median in the middle third of the forearm, although the division occurs distal to the origin of the main branches supplying the flexor sublimis digitorum and the anterior interosseous nerve. This is apparently due to the origin from the median trunk in the lower third of the forearm of a branch which supplies that portion of the flexor sublimis digitorum which flexes the proximal interphalangeal joint of the index finger. From a study of the number of patients with division of the median in the upper part of the forearm, where the precise anatomical level with regard to the origin of branches had been defined at operation, I am inclined to the view that a greater proportion of afferent fibres pass in the branches to the flexor sublimis digitorum than to the flexor profundus digitorum.

From personal observations it seems to be almost a rule that if any power to appreciate contact is retained in a part there is always in the same region some retention of the power to recognize pressure pain, although the amount of pressure required to induce pain may be very much greater than in the same region on the sound side. This latter

point is well illustrated by the following record, which also supports the previous contention that more afferent fibres are transmitted by the tendons of the flexor sublimis digitorum than those of the flexor profundus digitorum.

Patient, J. C. Complete division of the ulnar was found in the upper part of the forearm, just distal to the origin of branches for the supply of the flexor carpi ulnaris and inner half of the flexor profundus digitorum, which muscles possessed voluntary power. The loss of epicritic and protopathic sensibility corresponded to the full typical normal distribution. It was impossible to measure the error in the localization of tactile pressure over the little finger, as the best response to any stimulation he gave was "somewhere on my little finger," and he was quite unable to attempt to chart any of the stimulations in this region, although he invariably recognized that a contact had been made, provided sufficient pressure was used. The average of the three readings with the algometer on the two sides at four points may be conveniently tabulated for comparison.

	Sound side	Affected side
Hypothenar region	3.8	2.7
Between heads of 4th and 5th metacarpal bones	3.2	3.0
Over proximal phalanx of little finger ..	3.0	5.3
Over distal phalanx of little finger	2.0	7.0

It will be noticed that in the first two regions the reading was slightly lower on the affected side, whilst in the case of the two tests on the little finger the reading was markedly higher on the affected side, being more than three times greater on the distal phalanx.

Two other patients in whom similar results were found have been encountered. I have never seen "contact" and "pressure pain" completely dissociated. On the other hand these two forms of deep sensibility may be retained in a part without any power of localization being present, as in the little finger of the patient just referred to.

After division of the ulnar nerve at any point proximal to the origin of the branches for the supply of the flexor profundus digitorum, the area in which complete anæsthesia to all stimuli is found is very constant in extent and affects the little finger and the inner border of the hypothenar region as shown in fig. 6. After division of the median above the level of the branches supplying the long flexor muscles, the area of complete anæsthesia is by no means so constant. In sixteen cases of known complete division of the median, at or proximal to the level of the elbow joint, there was complete anæsthesia only of the index and a small neighbouring portion of the palm (fig. 7, A) in six; of the index and medius and a larger portion of the palm in five

(fig. 7, B) ; and the index, medius and palmar surface of thumb together with a still larger extent of the palm in five (fig. 7, C). The infrequency (only five out of sixteen) of complete anæsthesia of the palmar surface of the thumb was rather surprising, but the foregoing results were confirmed by the examination of a group of patients suffering from

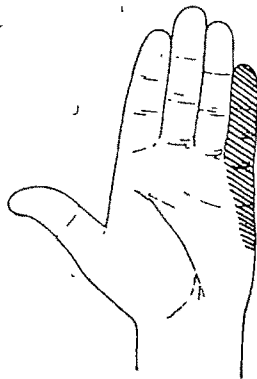


FIG. 6.—To show the typical extent of absolute sensory loss after division of the ulnar nerve in the arm.

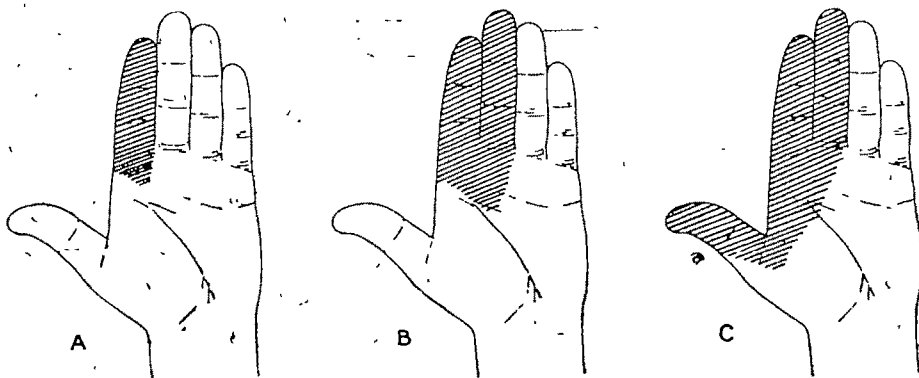


FIG. 7.—To show the variation in extent of the absolute sensory loss after division of the median nerve in the arm.

division of both the median and the ulnar nerves in the upper arm, in whom contact (if sufficient pressure was made) was recognized over the palmar surface of thumb in an even higher proportion. Consequently it must be surmised that the nerve, and possibly in a small number the communicating branches, takes

part in the innervation of the deeper tissues of the palm and the palmar surface of the thumb.

VII.—SUMMARY AND CONCLUSIONS.

In each section the main conclusions which may be drawn from the experiments and investigations are presented; it now only remains necessary to restate the principal conclusions bearing upon our present conception of sensation, and these may be conveniently summarized in three divisions.

(1) It seems clear that no nerve of sufficient size to be of clinical importance, or to be selected for experimental work upon sensation, is distributed exclusively to skin. Consequently after section of any of the nerve trunks, even in the distal part of a limb, there is bound to be some disturbance of so-called deep sensibility, and it seems quite impracticable to divide sensation into superficial and deep. Besides this anatomical criticism of such a division there is to be remembered the additional confusion which may arise from the knowledge that one form of sensation at least is transmitted by both cutaneous and deep nerves. It has been proved that so-called deep sensibility is not transmitted entirely by nerve fibres which accompany muscular branches, since the sensory supply of the joints of the fingers and thumb undoubtedly arises from the digital nerves, and it seems probable that other forms of deep sensibility are in part, at least, transmitted by branches arising independently from the main nerve.

(2) The various forms of sensation included under the division of deep sensibility may be dissociated. After division of the median at the wrist there is found a loss of the recognition of passive movements at the metacarpo-phalangeal and interphalangeal joints of the digits supplied by the nerve: some power of localization is retained over the region of the cutaneous distribution of the nerve, although by means of a measurable test a gross error is seen on comparing the results with those obtained on the normal part; the least pressure is readily recognized everywhere, and the readings with an algometer show that rather less pressure is required to induce pain on the affected than on the sound side. If division of the median occurs proximal to the supply of the outer part of the flexor sublimis digitorum in the lower third of the forearm, in addition to the defects just recorded there is usually a complete sensory loss over the distal two segments, and a small

proportion after section of the median at this level the loss of sensation in the index finger is less profound. Although in these there is no power to localize, the contact of pressure can be recognized and pain can be induced by excessive pressure, but on investigating the two latter forms of sensation more fully it is discovered that more pressure is required to induce the sensation of contact over the index than the medius and the reading with the algometer is considerably higher than on the sound index. The condition of what we know as deep sensibility in the index is, in such cases, in a most interesting stage and may be summarized as follows :—

- (i) Loss of sense of position and recognition of passive movement in all joints of this finger.
- (ii) Absolute loss of localization.
- (iii) Retention of recognition of contact and pressure pain, but on the application of measurable tests it is found that these forms of sensation are grossly affected.

Little reference need be made to the effect upon deep sensibility of a lesion at a higher level, in the region of the elbow or in the arm, since, except with regard to localization which has already been fully discussed, the condition is well known; reference is only necessary to the fact that the extent of the absolute sensory loss to all stimuli is variable.

(3) Observations upon the recovery of deep sensibility demonstrate several striking and significant features. Reappearance of the recognition of contact and appreciation of pain on the application of excessive pressure occurs early, as a rule during the stage of protopathic recovery. At first considerable pressure is required before it is appreciated, but the recovery of contact without concomitant recovery of pressure pain has never been encountered, although the extremely high reading with the algometer in two patients examined suggest that this is possible, and there does not appear to be any obvious reason why these two forms should not be dissociated. As regeneration proceeds less pressure is found to be required at subsequent examinations. As the recognition of contact and pressure pain improve there is usually a return of some power of localization, but it is very grossly defective, the error being much greater in regions where there has previously been an absolute sensory loss than elsewhere. Further improvement in localization and signs of recognition of passive movement of joints occurs very late, and not until there is evidence of recovery of epicritic sensibility. Most of my studies have

been upon patients who have had a secondary suture of the median or ulnar nerve, and under these circumstances any recovery of accurate localization or recognition of passive movements of joints is at the best very defective and frequently remains absent. After primary suture there is a better opportunity for studying the later phases of recovery. It seems very significant that recovery of recognition of contact and appreciation of pressure pain, followed often by a gross and defective return of the power of localization, occur early during the stage of reappearance of protopathic sensibility, whilst accurate localization and recognition of passive movement only appear late, at a time when there is also evidence of epicritic return as tested by graduated hairs and the compass. That is to say the three forms of sensation concerned with spacial recognition—accurate localization, discrimination and recognition of passive movement—only recover at a very late stage, and even after primary suture are apt to remain defective.

These observations upon the recovery of certain forms of sensation after suture of a peripheral nerve suggest two important facts.

(a) What we have regarded as deep sensibility ought to have been subdivided, just as cutaneous sensation has been divided, into epicritic and protopathic. There is no doubt that the two forms of sensation, recognition of the contact of pressure and appreciation of passive movement, must be subserved by nerve fibres terminating in the deep tissues; the former of these returns early at a time when protopathic sensibility is recovering, whilst the latter returns at a late stage, if at all, during the time of epicritic recovery. The mere recognition of the contact of pressure is a crude form of sensation compared with the more highly graded appreciation of the direction, localization and range of passive movement of a joint.

(b) In the light of Head's recent work upon the sensory cortex [2], these results suggest that at the periphery, both in cutaneous and deep tissues, we have cortical and thalamic aspects of sensation. The dissociation which is encountered after the division of any large nerve trunk makes it exceedingly difficult to unravel the fundamental principles upon which sensation at the periphery is based, but when we get an accurate conception of the anatomical distribution, and in the light of this knowledge analyse the results of careful clinical examinations of a number of patients suffering from division of a peripheral nerve, the curious forms of dissociation become more intelligible. Continued examinations of the same patients during recovery seem to bring us

still nearer to a knowledge of the true state of affairs. It has just been stated that certain forms of deep sensibility constantly recover during the early stage when the area of protopathic loss is found to be receding, whilst other forms do not show any recovery until a late stage when there is clinical evidence of a return of epicritic sensibility. In the examinations of a very large number of patients I have found this to be an invariable rule.

It appears to have been generally believed that the earlier return of protopathic sensibility is dependent upon a more rapid rate of regeneration in protopathic than epicritic fibres. Such an explanation supposes some structural difference in the two systems, and Ranson [4], on histological and experimental evidence, made the suggestion that impulses giving rise to pain travel in non-medullated fibres; but more recent work by Adrian [1] shows that it is highly improbable that there is any definite structural difference in the fibres concerned with protopathic and epicritic sensation. A simpler explanation is suggested when we take into consideration all the forms of sensation which return during the later stage of recovery. The forms appearing late, which more frequently show imperfect recovery, or in quite a proportion of cases of secondary suture fail to recover, are those which Head has proved to have cortical representation; whilst the forms which exhibit early and more constant recovery are those which may be expected to persist after destruction of the sensory cortex. Therefore it seems more reasonable to expect to find an explanation of the two stages of recovery in the central nervous system, rather than to find it due to a different rate of regeneration of two sets of fibres which anatomically appear to be identical. After suture and regeneration of a peripheral nerve a much longer period may be expected to elapse before the fibres subserving cortical forms of sensation function correctly, than in the case of the fibres conducting the thalamic aspects of sensation; since a very much more complex readjustment and re-education must occur after regeneration of the fibres in the former case than in the latter. Furthermore, on the hypothesis suggested in this paragraph, we seem to have ample reasons for the more constant and perfect recovery of such aspects of sensation, as cutaneous pain, pressure pain and appreciation of extremes of temperature, than for the higher forms, as those concerned with spacial recognition.

(The expenses of this research have been borne in part by a grant from the Royal Society.)

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TOXIC POLYNEURITIS.¹

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RECOGNITION of multiple or peripheral neuritis as a clinical and pathological entity dates from the publications of Duménil in 1864 [10] and especially of Leyden in 1880 [24]. Since that time a host of observers have studied the disease, so that the varieties of the commoner forms, the alcoholic, lead, arsenical and diphtheritic paralyses, are well known. It is not my intention to dwell on those forms the etiology of which is clear and unmistakable, but rather on the numerous lesser known types, the origin of many of which is quite obscure.

Multiple neuritis in our present state of knowledge is best classified on an etiological basis, rather than on pathological distinctions or clinical differences, and four main groups may be separated—

(1) Those dependent on the absorption of poisons introduced into the body.

(2) Those due to autotoxæmia, or to poisons developed primarily within the body.

(3) Those due to infections of an organismal nature.

(4) Those occurring in cachectic states.

The first group may usefully be divided into two sub-groups, those due to metallic poisoning, and those due to poisoning by various carbon compounds.

The term toxic polyneuritis has been much used, but, as probably all polyneuritis is dependent on some toxin, its employment seems most appropriate for those cases in which the infective agent or the source of poisoning is not clearly established. Before dealing with these a few examples of rarer forms from the different groups may be referred to.

Silver is a very rare and probably doubtful cause of polyneuritis, the

¹ Presidential address delivered before the Neurological Section of the Royal Society of Medicine, October 12, 1922.

only case in the literature appearing to be that described by Gowers [13], of a man of 44 who took a dinner pill containing silver for about twelve years, averaging six pills a month. After eleven years cyanosis commenced to develop, and a year later wrist-drop, though as carcinoma of the liver declared itself some three months later, it is possible that the polyneuritis was to be accounted for by the toxæmia from the malignant disease.

Carbon bisulphide is a sufficiently uncommon cause of polyneuritis to justify a short description of a case I have had recently under treatment.

A boy, aged 15, worked at a boot factory at solutioning on rubber soles. He worked in a shed, which was afterwards described by the inspector as very badly ventilated, using for the purpose of fastening on the rubber soles a rubber solution containing carbon bisulphide. He worked from 8 a.m. to 6 p.m., and began to feel unwell in July, 1921, when he commenced to suffer from headaches almost every night towards the end of his work. The headaches were accompanied by vertigo, but had disappeared by the following morning. He informed me that previous workers at the same job had had to give it up on account of similar headaches and giddiness. He, however, stuck to his work, and in January of this year his right leg began to feel weak and to give way when walking towards the end of the day. This improved, and then the right hand grew weak and lost the power of gripping; this also improved and the left hand became similarly affected. The headaches ceased in January just before the legs began to be affected. There was never at any time pain or numbness, or objective or subjective sensory symptoms. By the beginning of April he began to develop weakness of the dorsiflexors of both feet, being unable to raise the toes off the ground when standing, though the gastrocnemii were strong. Soon also bilateral weakness of the extensors of the fingers and wrists appeared, especially of the right extensor carpi ulnaris. Marked weakness and wasting of the right first dorsal interosseus and thenar muscles was also seen. To electrical testing there was well-marked reaction of degeneration in the extensors in both forearms, in the right first dorsal interosseus and in the tibialis anticus on each side. The knee-jerks were normal throughout, but the right Achilles jerk was absent, and the left only just obtainable with reinforcement. Treated with strychnine injections and massage he soon showed slight improvement, and after four months had practically recovered.

Carbon monoxide polyneuritis I have never met with, but it is said that a single severe dose of poisoning with this agent may be followed by neuritis, a very unusual feature in polyneuritis, which is usually the sequel of a more sustained or chronic poisoning. Care must, however, be taken in cases of carbon monoxide poisoning not to mistake pressure neuritis of the musculo-spiral, external popliteal or other nerve trunks

for toxæmic neuritis, pressure palsies being especially liable to occur in persons rendered unconscious by coal gas poisoning or by explosions in coal pits, through lying on a hard surface in one position for many hours.

Rheumatic polyneuritis.—Acute rheumatism or rheumatic fever is rarely if ever followed by polyneuritis, yet local perineuritis and fibrositis, as seen in brachial neuritis and sciatica, are common sequelæ of chill and exposure, though other causes frequently contribute, such as dental or intestinal sepsis.

Chloretone has been given extensively in children for chorea, and has been observed to produce a condition of flaccid paralysis, with absent deep reflexes, but the recovery on cessation of the drug is usually much more rapid than is usually met with in other forms of polyneuritis.

Local *asymmetrical neuritis* of definite nerve trunks rather than a symmetrical polyneuritis, is also a feature of typhoid and paratyphoid infections. Thus, a man of 29 with paratyphoid, a week after admission to hospital developed severe pains in the upper arms and shoulders, which kept him awake, followed by marked paresis of the right serratus, latissimus, triceps, and extensors of the right fingers and thumb, and of the left deltoid.

Another case of asymmetrical severe neuritis of the right median, ulnar and musculo-spiral nerves occurred in a man aged 27, as the sequel of a febrile attack of uncertain origin with tonsillitis, followed by acute nephritis. There was never any peeling of the skin to suggest scarlet fever, and bacteriological examinations for diphtheria, enteric and paratyphoid were negative. Possibly the infection was rheumatic, as nephritis is one of the rarer complications of this disease. After two weeks he had severe pains in the right arm from the shoulder to the hand, completely losing the use of the arm, and anæsthesia of the hand up to the wrist. The hand became very clawed and atrophic, and the finger pads and skin wasted, but practically complete recovery took place in two years. These asymmetrical forms of toxic neuritis are generally painful, perhaps owing to the inflammatory nature of the lesions affecting the interstitial tissue of the nerves, whereas in the symmetrical polyneuritis without sensory phenomena the lesion is probably purely a parenchymatous degeneration of the nerve elements themselves.

Asymmetrical neuritis of toxic origin may occasionally be met with in chronic alcoholism and diabetes. Musculo-spiral paralysis I have

many times seen occur in chronic alcoholism, when the element of pressure could apparently be excluded as a cause. In none of these cases of musculo-spiral palsy was pain a feature of the case, but in the sciatic and external popliteal paralyses met with in diabetes severe pain may be a prominent feature, preceding and accompanying the paralysis. It is difficult to understand how a local asymmetrical neuritis can be set up by the action of a circulating toxin, which should presumably act equally and symmetrically on both sides. The fact that certain whole nerve-trunk areas are liable to be affected in the asymmetrical forms is suggestive of a local interstitial neuritis being present rather than a degenerative parenchymatous neuritis, and this is further supported in my opinion by the fact that these asymmetrical forms are usually intensely painful. It is possible therefore, if not indeed probable, that the circulating toxin is not the direct factor in the development of the neuritis, but that it has led to the local appearance of an inflammatory interstitial neuritis, such as may result from chill and other so-called rheumatic processes.

The actual nature of the circulating toxin in such apparently simple cases as alcoholic or diabetic multiple neuritis is obscure. In all probability it is not alcohol itself or derivative ethers circulating in the blood that sets up alcoholic neuritis, or this disease would surely be commoner than it is, but rather a secondary auto-toxæmia produced by the action of the chronic alcoholism upon the tissues, notably on the digestive tract and the liver. Similarly in diabetes it can scarcely be the direct action of hyperglycæmia on the nervous structures that sets up local or multiple neuritis, nor is it due to acetone or diacetic acid, as both of these substances may be absent in cases of diabetic neuritis. Probably the neurotoxin in diabetes is of the autotoxæmic deficiency type, as will be referred to later.

The *polyneuritic psychosis* described by Korsakow [22] as common in chronic alcoholism with polyneuritis is certainly met with in other forms of polyneuritis, as Korsakow himself showed, and must therefore not be accepted as evidence that alcoholism is the cause of an obscure polyneuritis. Some two years ago I had the opportunity of watching throughout to its fatal ending a case of polyneuritis of unknown origin, in which the delusions and characteristic disorientation of time and space familiar in Korsakow's psychosis were very marked.

A man, aged 55, hall porter, early in September, 1920, began to suffer from severe pains in the left hip. After a fortnight he had to give up his work,

and three weeks later pains appeared in the right hip. On October 16, he was admitted under my care into St. Mary's Hospital as a supposed case of sciatica. There was some loss of power in both legs, and tactile anæsthesia of the feet and ankles, but no loss of power or of sensation in the arms or hands. Both knee-jerks and Achilles-jerks were absent, the plantars flexor. No glycosuria or albuminuria. Wassermann test of blood and c.s.f. both negative. On October 26, the electrical reactions were normal, but on November 5, definite reaction of degeneration had appeared in the left dorsiflexors, and peronei in both legs. By November 12, bilateral foot-drop was well marked, and there was retention of urine, daily catheterization being necessary. His mental condition had gradually become unreliable, and by this date delusions were very marked; he muttered to himself, and replied in the most extravagant manner to questions as to where he had been recently, such as to New York yesterday, and to Jerusalem the day previously, though he would otherwise answer questions quite rationally. He had always consistently denied the imputation of alcoholism, and I was able to convince myself by personal interviews with his wife and with his fellow employees at the Town Hall where he was porter, that his statements on this point were true. Irregular pyrexia developed towards the end of October, and he steadily got weaker and more torpid, dying on December 14. No post-mortem was permitted.

In another case, a man, aged 45, had a severe attack of polyneuritis, with intense pains in his feet and legs, with loss of the deep reflexes, and considerable delirium. Alcohol as a cause could be excluded. He later recovered all his muscular power, and the knee-jerks returned, but there was considerable permanent loss of memory and mental power, indicating the co-existence of an acute encephalitis with the polyneuritis.

Septicæmia is a not uncommon cause of multiple neuritis, differing little in type from alcoholic neuritis. The source of infection may be a quite insignificant wound; in two cases I saw well marked multiple neuritis follow slight local suppuration due to a grazed skin wound of the hand, and in another case due to a stab wound in the thigh. In one of them an early symptom was loss of ocular accommodation, which is such a common early symptom in post-diphtheritic neuritis.

Septicæmia is a not uncommon cause of multiple neuritis following childbirth or a miscarriage; one of the most severe and painful cases I have ever seen, ending in death from heart failure, occurred in an otherwise healthy girl of 23, after a miscarriage at three months, in all probability an artificially induced abortion. The polyneuritis which has been described as following tetanus is almost certainly of septicæmic origin; rather than due to tetanus toxin, though chloretone used in the treatment has been blamed in one case. I have seen the use of anti-streptococcal serum followed by a severe external popliteal paralysis; a

gunshot wound necessitated amputation of the foot, but on account of sepsis three doses of antistreptococcic serum were given on three successive days, and then after four days interval another dose. General joint pains all over resulted, followed four days after the last injection by pains in the right leg, dropped foot and wasting of the leg, with total paralysis of the extensor longus digitorum and of the peronei. It is doubtful whether this was septicæmic neuritis, or an effect of the serum.

Septicæmic neuritis may affect a nerve trunk close to the intervertebral foramina, as in a case of a gunshot wound of the left arm, followed four weeks later by pains in the opposite arm and right side of the neck, with paresis of the right serratus magnus and winged scapula, and hypo-æsthesia of a cutaneous strip from the ball of the thumb along the outer forearm and up to the shoulder, suggestive of neuritis of the sixth cervical nerve.

Generalized polyneuritis affecting all four limbs, with ataxy and loss of the knee-jerks, has been recorded by Clayton [9] in a soldier treated for typhoid by fifteen injections of 50 c.c. each of antityphoid serum. Here again it may be asked whether the polyneuritis was a result of the serum injections, or was it due to the typhoid toxin? My own view is that the neuritis is not the result of the serum treatment, but of the previous toxæmia, just as polyneuritis following diphtheria, whether treated with serum or not, should certainly be laid to the credit of the diphtheritic toxin.

A rare form of polyneuritis with facial diplegia has been described by Feiling [12] and others accompanying *parotitis* and *uveitis*, or polyneuritis may follow parotitis alone.

Acute febrile polyneuritis, first described by Osler [29], was frequently observed during the Great War, and cases were recorded by Gordon Holmes [21], Bradford [6], and others. The sequence of the polyneuritis to definite malaise and pyrexia places this type definitely in the infective rather than in the autotoxæmic group, though the exact source of the toxin has not yet been determined. Facial diplegia was a common symptom in this type of polyneuritis.

I saw a medical officer, just home from France early in 1919, who complained of pains in the left side of the neck, with soreness to touch, as though bruised, and almost immediately aching appeared in both forearms; three days later insomnia, and the arms became weak and the hands shaky. After three weeks facial diplegia developed, with a feeling of intense depression and malaise, with furred tongue, though no pyrexia was detected at any time.

There was a good deal of pain with hyperæsthesia and tenderness of the backs of the forearms, but no actual muscular paralysis. The knee-jerks were present throughout, and the legs were unaffected. There was never any sensory loss, and recovery was complete after three months.

Syphilis as a cause of polyneuritis is usually included in the cachectic group, but occasionally it undoubtedly acts as an acute infective toxæmia.

A man, aged 30, acquired syphilis in January, 1910. Three months later he developed some ataxy and numbness of the feet, but recovered. In October the numbness and ataxy returned with rapid onset of weakness of legs and arms, but again almost completely recovered under injections of salicylate of mercury. In January, 1911, twelve months after the original infection, weakness and wasting of the hands and feet began, which steadily progressed to complete paralysis of all muscles below the knees, with bilateral finger-drop and wasting of the forearm muscles.

All the deep reflexes were lost, but there was no trace of anæsthesia.

By November, 1912, he was recovering fair power in the gastrocnemii, and he could walk fairly with a stick. The hands were now normal, and the knee-jerks had returned, but there was no trace of power in any of the anterior tibial muscles, nor any reaction in them to either form of electrical current. Probably the correct interpretation of this case would be a polyneuritis associated with considerable anterior horn cell damage in the fifth lumbar region.

In considering the etiology of an attack of multiple neuritis in a syphilitic subject, the possibility of arsenical neuritis should not be overlooked if treatment by any of the arsenobenzol preparations has been given.

Tubercle as a cause of polyneuritis has been much discussed, the usual verdict being that such polyneuritis is mainly alcoholic, though the added stress of the tubercular toxin or cachexia, when combined with the chronic alcoholism, much increases the liability to degeneration of the nerves, just as alcohol in addition to arsenic, sepsis with rheumatism, and many other doubly acting causes may combine to produce it. Except when associated with another factor, tubercle is a very rare cause of neuritis. I have seen one case of generalized polyneuritis in a man dying from miliary tuberculosis, with no history of alcoholism or other ascertainable cause.

Tubercular neuritis of the feet.—In two cases of severe and fatal tubercular infection, I have seen symmetrical pains and wasting of the intrinsic musculature of the feet, with glossy skin. The first case had

been diagnosed as gout, in spite of extensive pulmonary tuberculosis, by no less an observer than the late Sir William Broadbent in 1895, and remembering this case when I saw the identical condition of the feet seven years later in a woman with obscure renal disease and pyrexia, I confidently diagnosed tubercle as the cause, though no one else agreed with me until the autopsy confirmed this.

In a few cases I have seen tubercular pleurisy followed by intensely severe *brachial neuritis* on the same side; with glossy skin and articular disorganization of the phalanges. Probably this is produced by apical infection of the lung and pleura setting up a secondary inflammatory neuritis in the brachial plexus in its close proximity.

Severe chronic anæmia is usually included among the *cachectic* causes of polyneuritis, though it appears to be much rarer than the spinal degenerations of combined sclerosis met with in conjunction with grave anæmia of pernicious type. I published last year [19] a case of *leukæmic polyneuritis*.

A youth, aged 17, developed well-marked symmetrical polyneuritis, with foot-drop, absent deep reflexes and sensory diminution on the feet and legs, as well as tingling and numbness of the finger-pads. His spleen was enlarged three finger-breadths, but there was no leucocytosis, indeed a leucopenia of only 5,800, but the cell count was notably inverted, the polymorphs being only 23 per cent. and the lymphocytes 68 per cent. Slight enlargement of the glands in the neck appeared, and one of these was removed for pathological examination, but was reported to be normal. Troublesome hæmorrhage from the wound continued at intervals, again suggestive of leukæmia, and he died six weeks after admission into hospital, three months after the first appearance of weakness of the legs.

Microscopical examination of the liver, kidneys and peripheral nerves showed these tissues to be infiltrated with lymphocytes; yet it is difficult to conceive that the symmetrical polyneuritis could be due to pressure of the lymphocytic exudation upon the nerve fibres; it was more probably of toxic origin due to some unknown form of autotoxæmia connected with the leukæmic process.

Malignant disease is also included amongst the cachectic group of polyneuritis, though it seems to be rare.

A year ago I saw a civil engineer, aged 69, who had been operated on seven years previously for malignant growth of the ascending colon, a short circuit being performed. He recovered well, and for years lived an ordinary life, travelling a great deal. In October, 1921, he thought he caught a chill; followed by pains in the left shoulder, arm and forearm, "like a rat gnawing it." The pains spread across the back of the neck and then affected the right

forearm, being so severe as to necessitate morphia. When I saw him in December there was complete paralysis of both triceps, and of the extensors of the fingers and ulnar extensors of both wrists, though the radial extensors of the wrists and the supinator longus of each side were normal; both serratus magnus muscles were very weak. There was a large mass in the right hypochondrium, which was shown at operation to be growth in the ascending colon with most extensive involvement of the liver. The legs were unaffected and the knee-jerks brisk; there was no glycosuria.

The distribution of the polyneuritis in this case was most unusual, with bilateral finger-drop and total paralysis of both triceps muscles, the legs being quite unaffected. The intensity and long duration of the pain were also striking features of the case. Possibly chill contributed to the onset of the neuritis, but the duration of three months with increasing symptoms was more suggestive of a continually acting toxin or cachexia, and is better explained by the extensive carcinoma from which he was suffering.

Autotoxæmia.—Perhaps the most interesting group of causes of polyneuritis is that I have labelled "autotoxæmic." We are constantly meeting with cases in which the closest investigation can elucidate no cause for the polyneuritis. One is tempted therefore to look upon them as autotoxæmic, though the Scotch verdict of "not proven" would be more correct.

An unmarried woman, aged 47, a school teacher, early last November began to suffer from burning pains in the legs, the feet becoming numb two months later, with loss of power of walking. There was some swelling of the hands due to rheumatoid polyarthritis, which also involved the left knee-joint. She complained of pins and needles in the fingers, and developed finger-drop owing to paresis of the extensor communis, and weakness and wasting of the intrinsic musculature of the hands. There was tactile anæsthesia and analgesia of the left hand up to the wrist, but no objective loss of sensation on the right hand, though she said it did not feel natural. There was complete left foot drop and some weakness of the right dorsiflexors. She could move the right but not the left toes. Though the right foot was much stronger than the left, there was much denser anæsthesia of this limb, extending to just above the knee. The knee-jerks were both brisk and equal, the Achilles-jerks were absent, and the left forearm flexor jerk absent too, though the right was brisk. After two months the pains in the legs increased considerably, and she complained of a curious subjective sensation "as though she had several pairs of legs in bed." This continued for several weeks. Now, after eleven months, there is some improvement in the muscular power of the legs, but she is still only just able to walk. There was a perforation of the nasal septum, suggestive in appearance of old syphilis, probably congenital, but the Wassermann reaction in the blood was negative.

It was difficult to assign the cause of this polyneuritis, though I incline to look on it as *rheumatic polyneuritis*, in view of the presence of painful multiple joint swellings, and the asymmetry and painfulness of the affection.

Beri-beri was at one time considered to be an infective polyneuritis due to a bacterial poison, but the more recent view ascribes it to a deficiency of vitamins in the diet, due to the eating of polished rice; the husk of the grain, which is thus lost to the diet, containing all the vitamins. Such a deficiency can act indirectly only, by setting up changes in the metabolic processes of the tissues, and thus probably the production of some insufficiently broken-down excretory product, which in the course of circulation affects the peripheral nerves, causing symmetrical parenchymatous degeneration. The process may be compared to that in diabetes, in which the lack of the normal internal secretion of the cells in the islands of Langerhans in the pancreas so alters normal metabolism that an excess of dextrose is produced in the breaking down of the muscular tissue. Yet it is probably neither the dextrose in the blood, nor the acetone or diacetic acid by-products, which are the actual toxic agent in producing the neuritis. In diabetic neuritis there may be symmetrical numbness and anæsthesia of the extremities, with loss of deep reflexes, but little or no muscular paresis, though there is well marked ataxy, the so-called diabetic pseudo-tabes. In another form the pains may be extremely severe, and the muscular paralysis well marked, often in the distribution of one sciatic, external popliteal or anterior crural nerve. Why a circulating toxin should thus set up an asymmetrical neuritis is hard to understand; it is usual to explain it by inferring a locally acting cause in addition, such as overuse or strain of the limb, or undue pressure on the nerve. In the asymmetrical neuritis of rheumatism or of paratyphoid fever, the asymmetry may be due to local involvement of the nerve sheaths by direct organismal infection, as in leprous neuritis, but in diabetes no organisms are known to be at work.

Puerperal neuritis.—Polyneuritis developing shortly after childbirth, or even during the puerperium, is sometimes considered to be a septicæmic neuritis, due to sepsis acquired during parturition, or to retained septic products in the uterus from a previous pregnancy. I do not think that this explanation will cover all the cases of polyneuritis associated with pregnancy, but rather that some are true cases of auto-toxæmia, the toxin which produces the polyneuritis being elaborated in the tissues as an abnormal by-product of the metabolism in pregnancy.

A year ago I had under my care for some months a young married woman aged 30, who ten weeks after childbirth complained of weakness of the legs and of numbness, and of pins-and-needles spreading in the feet and hands, followed by numbness of the abdomen and chest up to the neck. All the deep reflexes were lost, and she was unable to lift the legs off the bed; the extensors of the fingers also became weak, but the extensors of the thumbs and of the wrists were unaffected. Bilateral facial palsy and diplopia next appeared, followed by diaphragmatic palsy for several days.

There was deep tenderness of the calves and forearms, and well-marked anesthesia of the feet and ankles, but she never suffered from any spontaneous pains. There was never any pyrexia or recognizable sepsis after the childbirth. She recovered completely after four months.

Ten years ago Batten [5] showed at a clinical meeting of this Society a woman with recurrent paralysis and wasting of the hands and legs, with absence of the deep reflexes, the paralysis recurring after two confinements. Such recurrent paralysis will be referred to presently as having been observed in other cases of apparently autotoxic polyneuritis.

Pressure neuritis as a cause of paralysis following childbirth must be carefully distinguished from toxic polyneuritis, the nerve that usually suffers being the sciatic, and especially its external popliteal portion, from pressure of the foetal head upon it near its exit from the pelvis at the sciatic notch.

Cranial nerve paralyses are common as a sequel of ordinary pharyngeal diphtheria, the third, fourth and sixth nerves being commonly affected, and occasionally the seventh, fifth, tenth and twelfth. The loss of accommodation due to paresis of the ciliary muscle, that is such an early sign in post-diphtheritic palsy, I have also seen in septicæmic neuritis and in one other case of toxic polyneuritis. Walshe [43] has pointed out that the frequency of incidence of cranial nerve paralyses after diphtheria is dependent on the close contiguity of the source of the toxin in the pharynx, as, in cases of polyneuritis following accidental diphtheritic infection of an open wound of the trunk or limbs, cranial nerve paralyses are uncommon.

A definite syndrome has been claimed for *polyneuritis cranialis*, many observations being recorded of neuritis limited to several cranial nerves. Oppenheim [28] thinks these cases are usually due to a basal process involving the cranial nerves. Kinnier Wilson [44] showed at the Clinical Section a man who, after right-sided otitis media of three weeks duration, developed nerve deafness, of the right ear, right facial palsy, paralysis of the right half of the soft palate and of the right

vocal cord, glosso-pharyngeal anæsthesia and hemiatrophy of the right half of the tongue, with bilateral loss of taste.

Slow chronic polyneuritis is a term that may be applied to cases in which the symptoms gradually increase during many months. Pain is usually either absent throughout, or only trifling at the commencement, but the muscular paralysis becomes extreme, and there may be extensive atrophy.

In the case of a man, aged 31, the symptoms gradually increased during twelve months, commencing with pain in the calves and a tired feeling, after the appearance of some large purpuric blotches on the legs.

The legs gradually became enfeebled to the stage of total flaccid palsy, the hands and forearms not being involved until nine months after the commencement of symptoms. When I saw him seventeen months after the onset, there was practically complete palsy of the feet and legs, hands and wrists, with contracture of the feet and hands. All the deep reflexes were lost and there was considerable anæsthesia in the periphery of all four limbs. The sphincters were normal, and no cause suggestive of polyneuritis could be discovered. Wassermann test negative in both blood and cerebrospinal fluid.

A girl, aged 15, became gradually weaker during twelve months until all four limbs were totally paralysed: she could not raise the head from the pillow, the eyelids and lips were partially paralysed, there was weakness of the masticatory muscles, and the tongue was somewhat wasted. No sensory symptoms were present at any time except slight paræsthesiæ of the fingers at the commencement. All the deep reflexes were lost, but only slight muscular wasting occurred, and no contractures. No improvement was observable in spite of daily massage and electrical treatment until eighteen months after the onset, when she slowly began to regain power, and ultimately recovered perfectly in another two years.

The slow development of the symptoms in such cases strongly suggests a continuously acting toxin, rather than an acute poisoning, and one is driven to the supposition that an autotoxæmia is at work. In the girl's case at least the continual absorption of external toxins could be excluded, as her first symptoms occurred when at school in South Africa and advanced for three months at home some distance away, and she continued to get weaker for another nine months after being sent to England.

Relapsing and recurrent polyneuritis.—The commonest causes of recurrent polyneuritis are chronic alcoholism and lead poisoning, but recurrence is also met with in cases where the cause is obscure. F. G. Thomson, [42] recorded the case of a youth of 19 in whom weak-

ness commenced in the hands and feet five days after being thrown out of a sculling boat; within another ten days there was complete paralysis of all four limbs and of both sides of the face, with considerable weakness of the trunk muscles. The sensory symptoms were confined to slight numbness of the fingers and the soles of the feet. All the deep reflexes were lost and considerable wasting developed later in the muscles about the shoulders, forearms and legs, the extensors being chiefly affected. Recovery was complete in every respect in about two years. An interesting fact in the history was that this boy at the age of 5 years had had apparently a similar attack of motor paralysis affecting all four limbs, ending in complete recovery in eighteen months. The acuteness of the onset of the paralysis following the immersion is strongly suggestive of chill being the exciting factor, though his previous similar attack at the age of 5 seems to demonstrate a predisposition in his metabolic processes to the development of a neurotoxin, or possibly an excessive sensitiveness of his peripheral nerves to the action of such neurotoxin.

In lead poisoning it seems to be established that a recurrence of wrist-drop and colic may be dependent upon some slight cause, as a febrile attack or an irregularity in diet, in the total absence of any fresh source of lead absorption. This fact lends support to Mary Sherwood's suggestion [36], that the first attack of neuritis leaves the nerves with a lowered power of resistance to the assault of a fresh toxæmia.

Grocco [15] was the first to describe recurrent attacks of polyneuritis in the absence of any obvious cause such as lead or alcohol. Other reports of such cases have been made by Eichhorst [11], by Mary Sherwood [36], who described two cases from Eichhorst's clinic in Zurich, though her first case was that of recurrent palsy of the right arm only, and should scarcely be classed with other cases of generalized multiple neuritis. Ross and Bury [93] describe two sisters with recurring paralysis. Targowla [40] recounts the case of a woman who had three attacks of paralysis at the ages of 19, 27, and 39 years. Sörgo [37] described the case of a man who after three attacks of abdominal pain and constipation developed bilateral palsy of the arms, followed twelve months later by a recurrence of the paralysis and colic, and again eight months later following a chill, colic, severe pains, paralysis of the arms, weakness of the legs, loss of the knee-jerks, respiratory paralysis and death. Degenerative neuritis was found in

the peripheral nerves. The sequence of the paralysis to attacks of severe abdominal pains and constipation is suggestive of an enterotoxin having been the cause, and is strikingly similar to the mode of onset of the paralysis in acute hæmatoporphyrinuric polyneuritis.

H. M. Thomas [41] published a clinical lecture on Recurrent Polyneuritis, describing the case of a man of 28, who had five attacks of paralysis within six years. In his case chronic indigestion was a feature of the illness, and possibly here also an enterotoxin was the cause.

A somewhat similar case was published by Nattrass [27]; a boy aged 18 developed double foot-drop, loss of deep reflexes, and other signs of generalized multiple neuritis, who had had two similar attacks of paralysis lasting for several months, one at the age of 4 and the other at 17. A peculiarity in his case was enlargement and tenderness of the nerve trunks, especially of the median, ulnar and external popliteal.

Hæmatoporphyrinuric polyneuritis.—In 1908 my attention was first drawn to this curious syndrome:—

A woman, aged 47, was admitted to St. Mary's Hospital with pains in the abdomen, following a cold three weeks previously. Her pulse was 120, and the urine was noticed to be dark reddish coloured, hæmatoporphyrinuria being found on analysis. A week later she began to complain of pains all over her limbs and body, and it was found that she could not raise her arms to the level of the shoulder. The pains were worst in the arms and shoulders, but there was no anæsthesia. In five days she was unable to sit up or to feed herself. Insomnia became troublesome, and there was retention of urine, with overflow incontinence. The pains in her arms were so severe that she complained of feeling as if the skin was being torn off. The knee-jerks were present on admission, but were afterwards lost for some weeks. Three months later she could just hold out her arms, but there was still complete paralysis of the extensors of the fingers on both sides, with reaction of degeneration, though the extensors of the wrist and supinator longus were unaffected. Ultimately she recovered completely, the hæmatoporphyrinuria having disappeared before she left hospital.

It was not until February 1921 that I met with another case of this disease.

A man, aged 45, well nourished and living in perfect conditions in the country, apparently in perfect health except that he had always been obstinately constipated, was seized with pains in the back. Next day his urine was dark red coloured. The pulse was 60, and he now complained of severe pains around the loins and the front of the abdomen, at first thought by his doctor to be renal colic and then an acute abdomen, for which he was

sent into a nursing home and a surgeon fetched from London. The latter however, refused to operate, making a diagnosis of acute pancreatitis. All the next week his pains were severe, and he was said to be jaundiced, and to have bile in the urine. On the fourth day there was retention of urine requiring use of the catheter. After eleven days he became excitable and nervous, owing to which I was asked to see him. The pulse was then 100, the strength of limbs and trunk good, and he could stand and walk. The knee-jerks were normal, as were all the other reflexes. He complained of some paræsthesiæ of the trunk, and, taken with his excitable nervous condition and sleeplessness, I thought he was developing acute mania. There was no history of venereal disease and his cerebrospinal fluid was normal. Two days later I saw him again; he could still stand, but the knee-jerks were now absent, and there was no weakness or anæsthesia. He again had retention of urine, and on the doctor passing the catheter I was astonished to see that the so-called bile-stained urine was port wine coloured, an extreme example of hæmatoporphyrinuria. Three days later he complained of "deadness" of the chest and abdomen when touched, and large areas in this region were found to be analgesic. Paresis of the deltoids was now well marked, as well as weakness of the flexors of the hips, but no other weakness of the limbs. His rectal temperature was now for the first time slightly raised; two days later his temperature was 100° F. and the pulse 132. He was now much weaker, unable to turn in bed and to cough owing to weakness of the abdominal muscles. The constipation became more and more extreme, the diaphragm paralysed, and he died after an illness of three weeks' duration. Unfortunately an autopsy was not permitted.

Needless to say, in both these cases sulphonal and other drugs as a possible source of poisoning were excluded. In both acute abdominal pains were amongst the earliest symptoms, followed immediately by hæmatoporphyrinuria, pains all over, paræsthesiæ and paralysis, especially of the arms, loss of knee-jerks, retention of urine and insomnia. In neither of my two cases was vomiting noted.

Hæmatoporphyrinuria may occur with symptoms of acute illness quite unconnected with the taking of any drug; it was first described in a case of acute rheumatism by MacMunn in 1880 [26], under the name of urohæmatin.

Acute attacks are ushered in by severe pains in the abdomen and loins, constipation, and sometimes vomiting. Dark-brown to port-wine coloured urine is an early symptom, and the pains continue and may spread all over the trunk and limbs. The pulse-rate is raised to 100 or 120, but usually there is no pyrexia. Retention of urine and even incontinence may occur, and occasionally mental symptoms may be noticeable, such as general nervousness, excitability, or even delirium and epileptic fits.

Gunther's excellent article [17] quotes fourteen cases in the literature, in four of which severe paralysis rapidly developed, followed by death soon after the onset of the paralysis, the earliest recorded case being that of Ranking and Pardington in 1890 [31].

These observers described the cases of two single women aged 41 and 47, both living in the same house, who were both taken ill with hæmatoporphyrinuria within a week; both were extremely neurotic, dyspeptic and constipated.

In the first case the symptoms followed immediately after a large dose (20 gr.) of acetanilide had been given in three doses within four hours. Partial suppression and retention of urine, which was port-wine in colour, followed immediately, and death occurred a week later, the legs being paralysed for a day before death. Their second case developed no paralysis and recovered, though the symptoms otherwise were similar. It is difficult to believe the possibility of simple coincidence for such a rare condition as hæmatoporphyrinuria in these two cases, in the absence of some common factor, as a drug, of which however there is no record, except the excessive dose of acetanilide in the first case.

Schulte [34] described the case of a ship's cook, aged 35, who was seized with abdominal pains, hæmatoporphyrinuria, followed by typical multiple neuritis affecting the arms only, paresis of the deltoids, biceps, supinator longus, infraspinatus and the extensors in the forearms. The pulse was only 48, there was no pyrexia and the man recovered.

Bachlechner [2] has recorded a case of hæmatoporphyrinuria followed by symmetrical wrist-drop and foot-drop, with the reaction of degeneration, in which the paresis developed with two succeeding attacks of the acute symptoms; and Gunther [18] states that repeated attacks of the syndrome of acute hæmatoporphyrinuria may occur within a year, though in none of his own cases did polyneuritis develop.

L. F. Barker and Estes [3] observed a girl aged 18 with hæmatoporphyrinuria and polyneuritis which ended fatally after sixteen months. She passed dark urine for the whole of that time, and suffered from pain in the lower abdomen, recurring nausea and vomiting, vertigo and epileptic fits. Laparotomy disclosed a dilated pylorus and duodenum. Two months later, after complaining of severe pains all over, bilateral wrist and foot drop developed, with extensive muscular atrophy, including the intrinsic hand muscles. The deep reflexes were at first exaggerated but later lost, and she died four months later. At the autopsy there

was found great distension of the stomach and duodenum. A very interesting point in this case was that the family history disclosed the fact that four other members of the family seemed to have suffered similarly with hæmatoporphyrinuria and nausea with abdominal pains, one of her sisters having died after being ill for nine months with similar symptoms. The strong family tendency to these symptoms, associated with hæmatoporphyrinuria, is practically conclusive evidence of an autotoxæmia being the origin of the syndrome. In all probability an intestinal toxin is to blame. Barker and Estes regard the gastro-duodenal dilatation as primary, the toxæmia producing the hæmatoporphyrinuria and polyneuritis being secondary. In my second and fatal case the obstinate constipation was a striking and troublesome symptom from which he had always suffered, and it is suggestive that the toxæmia was intestinal in origin.

Gunther applied the term acute toxic hæmatoporphyrinuria to those cases in which the symptoms follow chronic poisoning by sulphonal, trional, tetronal, veronal or its derivatives. Lead, saffron and glycerine, are also said to produce toxic hæmatoporphyrinuria.

Hæmatoporphyrinuria resulting from the use of sulphonal was first observed by Stokvis [39], in the case of a woman who passed port-wine coloured urine after taking sulphonal for many months. Schulz [35] described a fatal case after taking 15 gr. of trional daily for one month, the symptoms being epigastric pain and vomiting, and followed by loss of strength two weeks later, hæmatoporphyrinuria appearing for a few days before death. Many cases of this acute sequel of chronic sulphonal or trional poisoning have since been published, and in about one-fourth of them acute paralysis has been noted. The syndrome closely resembles that of acute hæmatoporphyrinuria not due to drugs. Thus, severe abdominal pains, vomiting and constipation, are often prominent symptoms, recovery rarely happening when all these three symptoms are present. A typical case was described by Anson [1]. A woman, aged 35, after taking 30 gr. of sulphonal daily for three and a half years, developed acute abdominal symptoms, constipation, hæmatoporphyrinuria, intense pains in the legs, loss of knee-jerks, followed ten days later by marked weakness of the legs, increasing to total paralysis, the arms being later similarly affected. There was no anæsthesia, but incontinence of both sphincters until death. In this case no toxic symptoms appeared until the drug had been taken regularly for three and a half years, but in other cases the symptoms have come on acutely after even one or two doses of trional or sulphonal.

In Keith Campbell's case in 1897 [7], in the Royal Asylum, Perth, a domestic servant, aged 22, nervous and depressed, and suffering from constipation, was given two powders of 15 gr. each of sulphonal and phenacetin. Vomiting commenced four days later, and hæmatoporphyrinuria fourteen days after taking the drugs. Convulsions developed as well as nystagmus, progressive paralysis, loss of the knee-jerks, and death occurred thirteen days after the first vomiting.

Stockton [38] described a case of acute ascending paralysis with hæmatoporphyrinuria in a girl, aged 27, who, previously strong and healthy, became obstinately constipated, and twelve months later nervous, irritable and anæmic. She was given three doses of 5 gr. each of sodium salicylate and sulphonal. Vomiting set in, the pulse became slow and the urine claret coloured. Fifteen gr. of sulphonal was given, and next night a similar dose of trional, but both failed to induce sleep. Anæsthesia of the buttocks appeared, followed by incontinence of both sphincters, shooting pains in the legs, progressive paralysis and anæsthesia, the arms being last affected, and loss of the knee-jerks. Some power returned in the feet and legs but the arms remained totally paralysed, and there was total loss of sensation on the trunk and lower limbs. Doubtful optic neuritis was observed before death. No autopsy was obtained. In the discussion on this paper, Putnam [30] referred to a case of his own of increasing paralysis with hæmatoporphyrinuria following the administration of sulphonal, in which degenerative neuritis was discovered at the autopsy, the spinal cord being normal.

A case of hæmatoporphyrinuric polyneuritis following the use of trional was published in 1901 by Hart [20], in which recovery occurred. Trional differs from sulphonal only in the substitution of an ethyl group, C_2H_5 , for a methyl group, CH_3 . His patient was a woman, aged 50, who had taken much trional for a long time, when acute colicky abdominal pain with nausea and vomiting developed. There was no pyrexia, abdominal tenderness or distension. Five days later hæmatoporphyrinuria appeared, followed within a week by progressive paralysis of the extensors of the feet and wrists, with severe pains, anæsthesia and loss of deep reflexes. There was delirium and psychosis of Korsakow type. The pains in the limbs and abdomen were excruciating for a time, and limb contractures developed, followed by a slow recovery.

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ON MUSCLE TONUS.

DE BOER'S EXPERIMENT ON THE FROG.

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BY J. W. LANGEJAAN.

DE BOER'S experiment consists in cutting the rami communicantes which unite the sympathetic chain with the spinal nerves of the lumbar plexus. After their section the frog is fixed in a clamp by means of a hook through the nose, as was first done by Brondgeest. When hanging in this way the difference in position and in length of the two hind legs can be observed. In these experiments the frog was always intact, that is the spinal cord was not divided. According to de Boer the leg on the side on which the rami communicantes are cut is invariably more extended and slightly longer than that of the normal side, and he attributes this difference to a loss of tonus of the muscles of this limb. He states that the loss of tonus in this case is as complete as after the section of the posterior roots of the lumbar plexus. This effect, according to de Boer, is permanent, and he concludes that muscle tonus is governed exclusively by the sympathetic system, and that the impulses maintaining tonus reach the muscles by way of the rami communicantes.

The same experiment repeated on the cat has yielded similar results. The definition which de Boer gives of tonus is the same as that of Johannes Müller, Brondgeest, and the great majority of recent investigators, viz., a state of slight contraction of muscle.

In repeating this experiment I performed the operation as carefully as possible. The frog was rendered motionless by being wrapped in cotton wool and the needles which fixed the animal pierced the wool only. The intestines were always kept within the abdominal cavity and pushed aside by means of a little tampon moistened in Ringer's solution. The blood-vessels were spared as far as possible, especially the large vena dorso-lumbalis (Gaupp). Before reaching the rami communicantes, the parietal peritoneum must be incised and in most cases the kidney pushed a little aside. In this latter manipulation, as well as during the section of the rami communicantes, it is difficult to

avoid stretching the sympathetic chain and its branches. The stretching of these nerves increases and lengthens the period of shock following the section of the rami.¹ The same effect is produced by bringing the intestines outside the body in order to facilitate the operation; most observers have done so and consequently produced severe and prolonged shock of the spinal reflex arcs.

I have performed the operation in every case on the right side only upon male frogs of moderate size. The operation is much more difficult in *rana temporaria* than in *rana esculenta*, and in many other respects too the former is not so suitable for the experiment. I usually divided the rami communicantes uniting the sympathetic chain with the seventh, eighth and ninth spinal nerve trunks, but in some cases the sixth ramus was also sectioned, and in others the tenth.² The latter ramus is very slender and does not seem to influence the muscles of the hind limb. As the wound must be carefully sewn up, this part of the operation took approximately a quarter of an hour and consequently I never observed the animals earlier than ten to fifteen minutes after the section of the rami communicantes.

Rana esculenta survived the operation well for several weeks, after which the animals were then killed for the purpose of autopsy; *rana temporaria*, however, stood the operation badly, suffered from severe shock and often died within the course of a few days. I think this was chiefly due to the bad state in which the animals reached the laboratory during this year.

When a normal frog is suspended by means of a hook piercing its nose, its first act is a defensive movement. By placing its feet against the hook and then stretching its extremities with force, it tries to free itself from it. A small drop of a 3 per cent. solution of cocaine upon the wound through which the hook passes often suppresses these movements. As soon as the defensive movements cease flight movements appear. In *rana esculenta* swimming movements are more common, whilst in *rana temporaria* jumping movements prevail. In its natural state a frog performs two different kinds of swimming movements; ordinary swimming, that is symmetrical and synchronous movement of the four legs, and alternating swimming movements. As soon as the

¹ The term "shock" is used for that temporary suppression or depression of nervous function which follows immediately upon mechanical injury of some part of the nervous system.

² The spinal nerve leaving the cord between the first and second vertebra is reckoned as the first spinal nerve.

fore-part of the body meets an obstacle when swimming in the ordinary way the movements become alternate; then the extended right fore-limb is flexed and adducted to the chest, and the flexed and adducted left hind limb is extended with force. These movements alternate with the reverse movements of the contralateral limbs; they are slower and less strong than the symmetrical swimming movements. On reaching land this alternating movement insensibly develops into creeping. Alternate swimming is, therefore, the transition between swimming and creeping, or it is a creeping movement in water. The jumping movement is always symmetrical, consisting chiefly in a forced extension of both hind limbs. All these movements are slightly modified when the frog is suspended, but in general they are easily recognized.

In my experiments the hook that pierced the nose was not attached immediately at the clamp, but was held by another hook fixed into the clamp. This arrangement allowed rotation to occur round the vertical axis as soon as the animal executed a movement which was not strictly symmetrical. Most observers using the suspension method of Brondgeest seem to have attached their animals in a similar way, so that there is scarcely any doubt that the reflexes caused by these rotations hampered their observations. The rotation movements which occur in my arrangement have in general a small amplitude and a quickly increasing and decreasing angular velocity. The frog is said to rotate clockwise when the rotation is in the same direction as the hands of a watch placed with the dial plate upwards; when the movement is reversed we say that the frog rotates anti-clockwise.

Such a rotation stimulates both labyrinths simultaneously but not to the same degree. Clockwise rotation stimulates chiefly the left labyrinth, anti-clockwise the right. The two labyrinths act synergically in the reflex movements they produce; these are most marked in the hind limbs, but they occur in the fore limbs too. The movements of the hind limbs are chiefly extension and flexion; the extension movement begins with spreading of the toes, combined with forced extension of toes and foot, followed by extension at the knee-joint and later by abduction of the whole leg from the middle line, combined with a slight ventral adduction at the hip-joint. The flexion movement commences with adduction of the toes, associated with flexion of toes and foot; then flexion at the knee-joint, followed by adduction of the whole leg towards the middle line, and a slight dorsal adduction at the hip-joint. The extension movement of the fore limb commences with a

slight spreading of the fingers, followed by extension of the arm and abduction from the body. The flexion movement begins with a slight adduction of the fingers, associated with flexion of the arm and adduction of the whole limb against the chest. The reflex movements resulting from the rotation of the suspended animal are shown in the following synoptic table.

ANIMAL ROTATING ANTI-CLOCKWISE (RIGHT LABYRINTH CHIEFLY STIMULATED).

Right labyrinth	Hind limb	{ Right, forced extension. Left, flexion.
	Fore limb	{ Right, extension. Left, flexion.
Left labyrinth	Hind limb	{ Right, extension, weak or absent. Left, slight flexion.
	Fore limb	{ Right, extension, weak or absent. Left, slight flexion.

When the animal rotates clockwise it is the left labyrinth which is chiefly stimulated, and the resulting reaction may be deduced from the table by interchanging right and left.

The movements elicited reflexly from the labyrinths are rather slow and are executed with considerable force. They commence in the toes and foot of the same side as the labyrinth which is stimulated by the rotation, so that when the animal turns clockwise it is the toes of the left foot which first spread. If the stimulus is weak, or the threshold high owing to the exhaustion of the reflex, the only obvious reaction is the spreading of the toes, the slight extension of the limb often escaping our attention.

The reflex elicited by the rotation of the suspended frog was first described and recorded photographically by Dusser de Barenne [7], who proved its labyrinthine origin. This reflex must not be confounded with the automatism provoked by suspending the frog by means of a twisted string, so that the animal turns slowly and always in the same direction. Like all reflexes in the suspended animal, the rotatory seems to be a normal reflex, for if we imagine the animal in its natural position with its four legs touching the ground the extension of the limbs of one side would check rotation round its cranio-caudal axis. According to the researches of Quick [16], this is the normal reflex movement elicited in all vertebrates by stimulation of the semicircular

canals. The rotation reflex is therefore probably a normal labyrinthine reflex, slightly modified by the suspended position of the animal.

When the animal has been suspended for some time, the irritability of the semicircular canals is increased owing to the abnormal position, and consequently even a slight degree of rotation is followed by a reflex movement. It is not possible to eliminate the reflex by suspending the frog by a single hook, since rotation may still occur owing to the elastic nature of the tissues in which the hook is fixed; under these conditions the excursions are greatly diminished and easily escape our attention, and we may be therefore deceived by the reflex movements provoked by them.

When the intact frog is suspended the defence automatism is the predominant reaction, and when it is eliminated the rotary reflex usually prevails. As soon therefore as flight movements produce a slight rotation of the animal, they are suppressed by the rotation reflex. If the spinal cord of the frog is divided between the second and third spinal roots the defence and the rotatory reflexes are abolished, and the flight reflexes prevail. The swimming and jumping movements, however, have no longer the same precision as in the intact animal, and are often arrested before the apparent aim of the movement is attained; in other words, the automatism subsides into a simple sequence of spinal reflexes.

It has been pointed out that the difference in the position of the two hind limbs may be rendered more evident by immersing the frog in water. Water being a dense medium of approximately the same specific density as the tissues, the tensional stresses existing in the muscles have free play to develop their strains when the animal is immersed. But water, in consequence of its density, also restricts movements, which consequently either do not occur, or cease earlier than they would in air. But the reactions observed when the suspended frog is immersed may not be the normal ones, since the immersion may act as a physiological stimulus. If the frog is lowered slowly and at a uniform rate and no farther than the middle of its body, into water of exactly the same temperature as the room, the immersion seems to have no stimulating effect, but if these precautions are neglected swimming movements are often elicited. Immersion into water of much lower temperature than the room seems to increase the flexion of the hind legs, but not to influence extension. This method therefore introduces many sources of error and cannot be considered an improvement. The suspension of a normal frog by a hook is also an unsatisfactory

method, and I should not have employed it if the question whether efferent sympathetic nerves influence the tonic state of the muscles had not been raised by de Boer's experiments performed by it.

In an earlier publication [10] I tried to show that muscle tonus depends upon two different properties of muscle, and that these two properties are governed by two different sets of efferent nerves. Shortly afterwards and independently, Pieron [14] [15] came to the same conclusion. The first property of the tonic muscle is plasticity. A body is said to be plastic if its form is permanently altered when a stress to which it is subjected is removed. It follows from this definition that if the body was in a state of equilibrium before the deformation, it will be again in equilibrium after the deformation. If, therefore, the form of a plastic muscle is altered for a moment by the action of internal or external forces, the deformation produced by these forces is partly permanent. The greater the permanent deformation in comparison with the total change of form, the more plastic the muscle. Hence, if a muscle contracts a shortening remains, while if it is extended by the action of its antagonists a lengthening is the result; whereas a muscle which has lost its plasticity returns after each change of form to the same definite length. It is evident that a permanent deformation in a muscle is not attended by a continued expenditure of energy nor accompanied by rhythmic electric phenomena, while the production of a permanent deformation, or a variation in an existing deformation, is accompanied by the expenditure of free energy and by electric phenomena¹. Plasticity, I believe, is intimately connected with what is usually called the "trophic state" of the muscle, and the degree of plasticity may possibly therefore prove to be a measure of the trophic state of muscular tissue.

Plastic tonus is that state of the muscle in which it has the properties of a plastic body. This term is chosen to indicate that the plasticity of muscle is maintained and controlled by the central nervous system. As shown in an earlier publication [7], an isolated muscle may be deprived of its plasticity by physical disturbances of the same kind as occur during the normal function of the muscle. There is, therefore, no doubt that the maintenance of plasticity is a function of the central nervous system. Hence, plastic tonus is a reflex tonus. It shows itself not so much during movement as after movement. It influences therefore the attitude of the animal, and its diminution or

¹Electric phenomena have been observed by de Meyer [12] in non-permanent deformation of muscle.

loss must alter normal postures. Sherrington, especially [17] in his article on reflex postural activity, called attention to this function of the tonic muscle. During movements plastic tonus influences the steadiness of the movement, and its diminution or loss is revealed by unsteadiness of movement.

The second property of the tonic muscle is the faculty of maintaining a state of slight contraction. This property of muscle I proposed to call *contractile tonus*. It is the reflex tonus of Johannes-Müller, Brondgeest, de Boer and of most of modern authors; it is now generally admitted that it is maintained and controlled by the central nervous system. When in a state of contractile tonus the muscle is not in equilibrium, but in a state of slight contraction. For this reason the maintenance of the contractile tonus is accompanied by the expenditure of free energy and by rhythmic electric phenomena; and it is therefore intimately connected with heat production, especially in the homoiothermic animals. The view that reflex tonus comprises two components is in harmony with recent morphological researches of Boeke [1], as well as with the researches of Wertheim Salomonson [18] on the electric phenomena of tonic muscle.

In order to avoid confusion, I will use the word "tonus" as the general term, comprising the two components, plastic and contractile tonus. The part played by each of the two components in the joint results is left indeterminate. The terms "plastic tonus" and "contractile tonus" will always be used strictly in the sense defined above.

The first group of experiments was made on intact frogs, the spinal cord not being cut. The seventh, eighth and ninth rami communicantes were divided on the right side. As soon as the animal is released, a quarter of an hour after the operation, it immediately regains its natural position and jumps away; when placed in the basin it swims. The voluntary movements seem almost normal, but the animal, when jumping or swimming, often deviates a little from the straight line. On squatting immediately after having made a jump, the attitude is abnormal (fig. 1). The trunk deviates to the left, the right hind limb is abducted from the body, the knee points laterally and the foot is not covered by the leg; the area of the limb in contact with the ground is larger than on the normal side. It is evident, on examining the mid-dorsal line, that the superior part of the trunk forms an obtuse angle with the inferior part. Below the level of this angle on the right side the papillæ of the skin are flattened and the skin itself is darker. On

the photograph reproduced in fig. 1, these changes, characteristic of loss of function of the sympathetic system, are very striking upon the trunk, but they exist also, though less distinctly, upon the right hind limb. When the animal sits quietly the curvature of the trunk gradually diminishes in the course of some minutes, but a slight deviation remains. The abnormal position of the hind limb is usually also corrected, but as this correction takes place abruptly it gives the impression of volitional movement. The slight deviation of the trunk at rest persists for a period of four to six weeks, and then disappears in



FIG. 1.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side; photograph on the following day to show the attitude of the animal three minutes after having made a jump.

consequence of gradual compensation, which may go so far as to lead to slight deviation of the trunk to the opposite side. As I will show later, it is impulses emanating from the left labyrinth which bring about this compensation. As soon as the frog comes to rest and floats upon the water after swimming, the right hind leg is not adducted to the body, but remains partly extended and hangs down (fig. 2). Sometimes extension is the most striking feature, at other times it is drooping of the leg. In consequence of this abnormal attitude, the frog no longer floats symmetrically, but the right half of the body, and especially its posterior part, is more submerged. When floating quietly this abnormal position may persist for a long while, but it is usually

corrected, apparently volitionally, in the course of some minutes. The abnormal attitude of the hind limb is permanent and may be observed for several weeks after the operation (fig. 3); complete



FIG. 2.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on December 27, 1921. Photographed next day as the animal floated on water. The right side of the body is more deeply submerged, and the right hind limb hangs down.

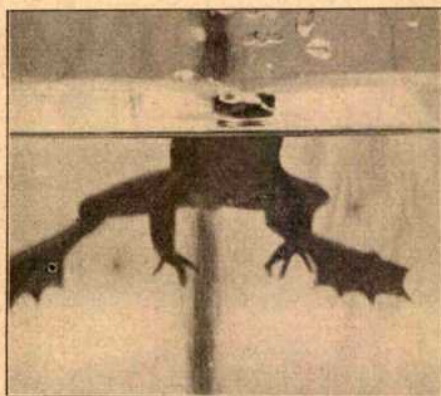


FIG. 3.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on January 4, 1922. Photographed on January 28, 1922, as the frog floated in water; front view. The right half of the body is more deeply submerged, and the right hind limb is more extended and hangs lower. Same animal as in fig. 4.

compensation did not occur in the course of my experiments. These different abnormal postures are easily observed in *rana esculenta*; in *rana temporaria* they are often absent shortly after the

operation in consequence of local shock, and later they are mostly obscured by the restlessness and lively movements of these animals.

When the frog is suspended immediately after the operation¹ the right hind limb is extremely flabby, more extended and slightly longer than the normal one. The flabbiness of the limb is the most striking phenomenon and is always present. It may be demonstrated by quickly moving the frog to and fro; then the right limb swings more easily, the amplitude of its movement is larger and it continues to swing after the normal limb has come to rest. If jerked up and down its movements are irregular, whereas the normal limb moves more smoothly. The flabbiness of the musculature is also shown by the form of the leg (fig. 5). The calf is flattened and the pretibial muscles hang down along the bone so that their greatest prominence is slightly lower than on the normal side. Similar differences may be observed between the two thighs. The flabbiness of the hind limb gradually diminishes in the course of the first day after the operation, but then remains approximately unchanged for at least two months. What happens after this period I do not know.

On comparing the attitudes of the hind limbs when the frog is suspended during the first hour after operation, it is evident that the right limb is more extended and that the right foot droops. The increase in the length of the limb is chiefly due to this abnormal position of the foot. When measured by means of a horizontal microscope it amounts to approximately 3 to 4 mm. in a middle-sized frog of about 185 mm. in length from nose to toe. In some cases the difference may reach 5 mm. immediately after the operation. If the animal is then carefully immersed in water the difference in the position of the legs becomes more obvious, and the flabbiness of the limb is more evident, for even the slightest vibration of the fluid is communicated to it, whilst the normal leg remains at rest. Some time after the operation the difference in position and in length of the two legs begins to diminish. If the operation was performed carefully recovery sets in within an hour, but if done roughly it may persist several hours. At the end of the first day, a state is usually reached which seems stationary for several days, till compensation becomes perceptible. In this stage, the difference in length between the two legs amounts to 1.5 to 2.5 mm. when the animal is hanging quietly.

¹ The descending root of the nervus trigeminus reaches the lumbar region of the cord in the frog. If, therefore, the hook piercing the nose deviates a little from the middle line, e.g., to the right, flexion reflexes may be evoked in the right hind limb by stimuli emanating directly from the wound made by the hook.

In experiments in which the operation happened to be easy and stretching the sympathetic chain and the rami communicantes could be avoided, I observed that immediately after the operation the right limb was more flexed and shorter than the normal one, but in the course of the first hour it became slightly more extended and longer than the left as the animal was hanging quietly. In these cases the final elongation never exceeded 2.5 mm. I am inclined to believe that in this instance the local shock was very slight, and that the section of the rami communicantes may have acted as a stimulus.

As soon as the frog is suspended immediately after the operation it usually makes defence movements. When this reaction to its abnormal position has ceased spontaneously or is suppressed by a drop of cocaine solution, the rotatory reflexes and those elicited from the skin are either abolished or strongly diminished on the right, and often slightly depressed on the normal side too, in consequence of the local shock produced by the section of the rami communicantes. The degree of depression of the reflexes depends chiefly upon the manner in which the operation was performed; if easy the depression is slight and of short duration; if, on the other hand, difficult and attended by stretching of the sympathetic chain, the depression is deep and prolonged. The first reflex that can be elicited is always the rotatory reflex. It reappears during the first hour after the operation and long before the stationary state is reached, in which the elongation of the right hind limb amounts to no more than 1.5 to 2.5 mm. It is evident, as the local shock is disappearing, that the reflex movements provoked by the stimulation of the right labyrinth are diminished, so that the movements evoked from the left labyrinth become preponderant. The depression of the function of the labyrinth on the side on which the rami communicantes are cut remains permanent during the whole period of observation, and one gets even the impression that the predominance of the left labyrinth increases rather than decreases. A glance at the table on p. 437 will make it clear that the predominance of the left labyrinth causes extension to prevail in the left hind limb and flexion in the right hind limb (fig 4). Moreover, the abnormal position of the animal increases the irritability of the labyrinths, so that even the slightest and hardly perceptible rotation provokes a reflex movement. As a result of the manner in which the animal is suspended there is probably no active movement which is not accompanied by a rotatory component, and the labyrinths are therefore incessantly stimulated. The rotatory reflex, as already said, is strongly dominant, and therefore after each active

movement of the animal the right limb is temporarily shortened and the left limb temporarily extended. This is the reason why Dusser de Barenne [6] observed shortly after the operation that the hind limb on the side on which the rami communicantes are severed is shorter than that on the normal side. It is only during the period of local shock, when the rotatory reflex cannot be elicited, or at the moments when the labyrinthine reflexes are exhausted, or, finally, when the animal has been hanging quietly for at least a quarter of an hour, that the elongation following section of the rami communicantes

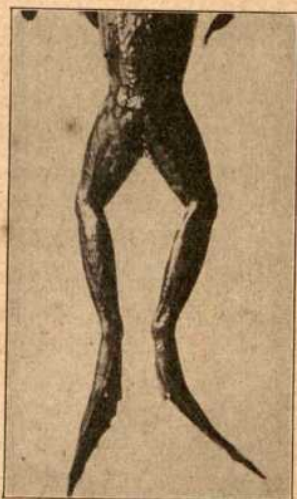


FIG. 4.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on January 4, 1922; photographed January 25, 1922. The flexion of the right hind limb when suspended is due to predominance of the left labyrinth. The same animal is shown in fig. 3.

can be observed in the frog in which the spinal cord is intact. I have also tried to demonstrate the difference in function between the two labyrinths by placing the frog upon a rotating disk. The correction movements, however, are chiefly executed by the head and those parts of the trunk lying above the level where the rami are divided. The method afforded, therefore, no definite results.

The reflexes that return next are those elicited from the skin. The first to appear is the simple flexion reflex, quickly followed by swimming movements, especially in *rana esculenta*, and by jumping movements in *rana temporaria*. The swimming and jumping movements often appear quasi-spontaneous. From the first moment that all these reflexes

reappear, it is evident that the movements of the right limb lack steadiness; they resemble in this respect the movements in locomotor ataxia. This unsteadiness is a consequence of the diminution of the plasticity of the muscles, and may be observed for at least several days after the operation. For the same reason the deformation of the muscle after a contraction or after stretching is diminished on the right as compared with the normal side. The right hind limb, having executed a movement, returns, therefore, more nearly to its inherent equilibrium length than the normal one. It follows from these considerations that the difference in length of the two hind limbs, as soon as the local shock has passed away, is not a fixed quantity, but depends chiefly upon what happened just before the limbs were at rest. Owing to the predominance of the rotatory reflex the right hind limb is more likely to be shorter at a moment arbitrarily chosen than the normal one. This fact was actually observed in the frog by Yas Kuno [9] and by Negrin y Lopez in co-operation with von Brucke [10], in the cat. It was erroneously considered by these observers as being in contradiction with de Boer's observations.

Summarizing the result of this group of experiments, we conclude: *Section of the seventh, eighth, and ninth rami communicantes in the frog is followed by local shock of the primary reflex arcs of the spinal cord. During the period of shock, the loss of tonus is complete (de Boer [2]). As soon as the shock has passed off the loss of tonus is only partial (Dusser de Barenne [6]). As a result of section of the rami communicantes, the muscles lose a great deal of their plasticity. The diminution of the plasticity of the muscles shows itself most distinctly in the attitudes of the animal, but the movements also lack steadiness. The results of diminution of plasticity are gradually compensated by stimuli emanating from the labyrinths, especially from the labyrinth opposite the side on which the rami communicantes are divided.*

The second group of experiments was also made on intact frogs. In this group, the seventh, eighth, and ninth posterior roots were divided on the right side. As soon as the animal is released, approximately a quarter of an hour after the section of the roots, it regains its natural position. The attitude of the animal is normal, with the exception that the right hind leg is flabby and trails behind the body in consequence of local shock produced by the section of the roots. In the course of the first half-hour after the operation the leg begins to flex slightly and

to adduct a little to the body. When in this period of recovery the animal floats upon the water in a basin, the hind limb is flexed, and brought almost into its normal position. At the end of the first day the right hind limb is still a little flabby. When the animal is squatting, the hind limb, in consequence of this flabbiness, projects a little from the body, and a greater surface of the leg touches the ground than on the normal side. Owing to the same reason the right heel is lower than the left. Sometimes the leg is more flexed than normal at the knee and the ankle joints, especially when the animal sits after having made a jump. This deviation from the normal position occurs only after the movement described by Hering [8] as the "tilt phenomenon." If the operation has been successful and local shock slight, the state of the animal immediately after it is approximately the same as it usually is at the end of the first hour.

When the animal is suspended directly the operation is terminated, the position of the right hind limb, as de Boer has stated, is exactly the same as it is after section of the rami communicantes. The difference in length between the two legs amounts at most to 5 mm. in a frog of normal size. This agreement in position and in elongation is due to the fact that in both instances the operation produces a severe local shock of the primary reflex arcs of the spinal cord, in consequence of which there is temporarily a complete loss of tonus. In the course of the first day after the operation, the difference in the position and length of the two legs diminishes, and finally the length of the right hind limb does not exceed the length of the normal one by more than 1 to 2 mm. This difference is still present a week after the operation. The rotatory reflex reappears within the first half-hour. At first the flexion and the extension of the right limb are somewhat feeble, but soon the difference between the reflex movements of the two sides is hardly perceptible. When the operation has produced but little shock, the rotatory reflex may be present from the first moment, and movement is almost normal—the only difference between the two sides being a slight diminution of the steadiness of the movement of the right limb. This unsteadiness is only perceptible during that phase of the reflex movement in which the foot is extended and the toes spread. When the animal has been suspended for a time even the slightest rotation provokes a reflex movement. This proves that the labyrinths become more irritable owing to the abnormal position of the animal.

Summarizing the results of this second group of experiments, we

may conclude: *Section of the seventh, eighth, and ninth posterior roots in the frog is followed by local shock of the primary reflex arcs of the spinal cord. During the period of shock the loss of tonus is complete, as Brondgeest has stated [4]. As soon as the shock has passed off, a diminution of tonus remains. The postures and movements of the animal are approximately normal, so that the diminution of tonus seems chiefly, though not exclusively, due to a decrease of contractile tonus. The rotatory reflex is not permanently influenced by section of the posterior roots.*

The third group of experiments was made on frogs in which the spinal cord had been divided between the second and third spinal roots. When the animal is released, approximately ten minutes after the section of the cord, it usually regains its squatting position when put upon the table in the proper manner. Its posture, however, is more crouching than it was before. Recovery from shock begins in the course of the first day after the section, and then the reflexes gradually reappear. When the animal is suspended, the loss of tonus produced by the shock is complete in the distal part of the body; the hind limbs are flabby and the heels often touch each other. As soon as recovery sets in the tonus returns, at first in the more proximal parts of the limb, later in the foot and the toes. The reflexes that may now be elicited are the flexion and swimming reflexes. The irritability of the preparation increases as the shock passes off, so that the slightest touch of the skin, or even an insignificant jar, elicits a reflex. Flexion movements now prevail, since the extension reflex emanating from the labyrinth is abolished. In consequence of the predominance of the flexion movements the permanent deformation of the muscles is in the same direction, and so the well-known flexion contractures develop.

When the shock following the section of the spinal cord has largely subsided, approximately twenty-four hours after the operation, the seventh, eighth and ninth rami communicantes are divided on the right side. The local shock following the section is usually not so severe as when the cord is intact. The phenomena which may be observed in the suspended animal are qualitatively the same as when the cord is intact. When tonus returns the right hind limb remains flabby and is slightly longer than the normal (fig. 5). The difference in length, however, never exceeds 1 to 1.5 mm., and usually amounts to 1 mm. only. As this slight difference in length is not very obvious, it is the flabbiness of the hind limb and the unsteadiness of its move-

ments which more clearly reveal the diminution of plasticity. The flabbiness of the limb, though diminished, still exists on the tenth day after the operation; I did not observe the animals for a longer period. The unsteadiness may be demonstrated by gently squeezing the two feet simultaneously; then the hind legs are raised and adducted to the body as if the frog were sitting, but the right limb is not so much adducted as the left, and falls abruptly when giving up this position. The left hind limb maintains the position somewhat longer and then falls slowly, often by steps. When the right leg is actively extended



FIG. 5.—The spinal cord was transected 1.5 mm. below the *calamus scriptorius* on January 9 at 1 p.m. At 1.30 p.m. division of the sixth, seventh, eighth, ninth and tenth rami communicantes on the right side. Photographed at 1.30 p.m. on the following day to show the difference in position and length of the hind limbs when the animal was partly immersed in water. The right limb—and especially its distal part—is surrounded by a halo, owing to slight vibration transmitted to this limb from the water; it affected this limb only.

the movement is also abrupt, and the leg often passes for a moment its position of equilibrium. On stimulating the two feet simultaneously, I often got the impression that the right limb, the rami communicantes to which were divided, was not so irritable as the other. I sometimes observed a slight, hardly perceptible flexion of the left leg occurring to all appearances spontaneously; and while in this flexed position, which may be maintained for several minutes, the reflex irritability of

the leg was considerably increased, so that even touching the foot with the point of a fine human hair provoked a vigorous flexion reflex. I have the impression that this slight flexion of the leg is the same phenomenon as the shortening of the muscle which always precedes a muscle clonus [11]. In both instances, I believe, the shortening is due to impulses reaching the muscle from the sympathetic system. In several experiments the succession and the interval of time between the two operations was varied, but the chief results were always the same.

Summarizing the results of the third group of experiments, we may conclude: *Section of the spinal cord between the second and third spinal roots is always followed by severe shock in the distal part of the body. During the period of shock the loss of tonus is complete, and when the shock has passed, a diminution of the tonus remains. Subsequent section of the seventh, eighth and ninth rami communicantes produces a diminution of the plasticity of the muscles of the hind limb. After the section of the spinal cord, the rotatory reflex is abolished.*

The fourth group of experiments was made on frogs in which the spinal cord was only partially cut through. The experiments in which the section of the spinal cord between the second and third spinal roots was proved by autopsy to be incomplete, taught that the rotatory reflex, though feeble, may still be elicited if the external part of the antero-lateral tract and the zona marginalis only are left intact. A certain number of fibres subserving the reflex reach, therefore, these regions of the spinal cord at the level not below the second spinal nerve.

In another set of experiments the more lateral region of the medulla oblongata, 1.5 mm. above the calamus scriptorius, was cut through on one side. The more medial region of the oblongata, containing the fasciculus longitudinalis posterior, was always spared. I divided therefore the formation known in the higher vertebrates as the corpus restiforme. The effect upon the posture of the animal resembles that produced by the section of the rami communicantes, but is much more pronounced and extends over the whole side of the body on which the corpus restiforme is divided, so that when swimming or jumping the animal deviates considerably from the straight line, and when squatting the whole body is curved to one side. The rotatory reflex emanating from the labyrinth on the side on which the corpus restiforme is injured is abolished.

Summarizing the results of this fourth group of experiments, we may conclude: *The fibres conducting tonic impulses from the labyrinth to the muscles pass by the way of the corpus restiforme; a certain part of the fibres subserving the rotatory reflex enters the tractus antero-lateralis of the spinal cord.*

The results of this research have led to a scheme of the primary spinal reflex arcs which differs from the current conception. While I was completing this scheme, Bok [3] published his morphological researches

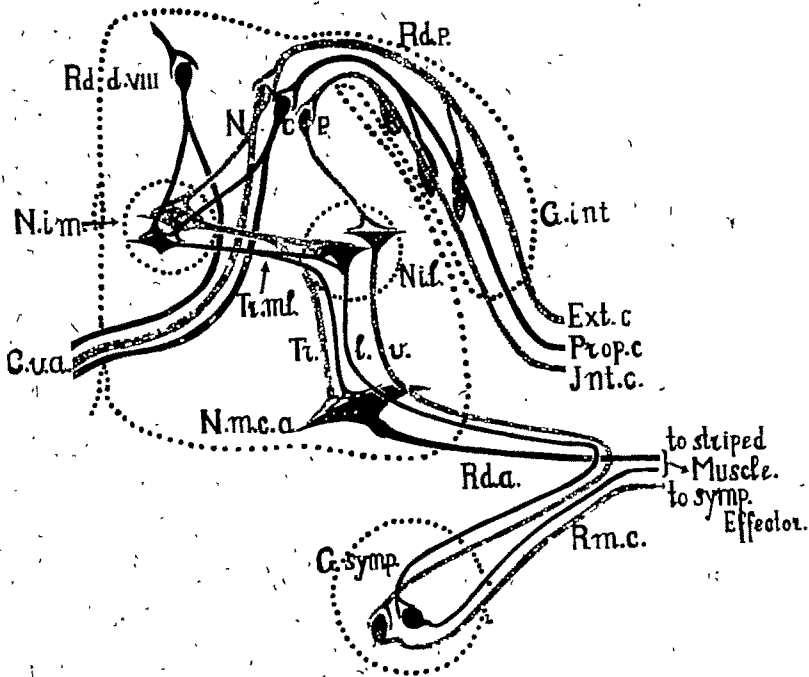


Fig. 6.—Scheme of the primary spinal reflex arcs. O.v.a., commissura ventralis alba. Ext.c., exteroceptor. G.int., ganglion intervertebrale. G.symp., ganglion sympathicum. Int.c., interoceptor. N.l., nucleus intermedio-lateralis. N.i.m., nucleus intermedio-medialis. N.m.c.a., nucleus motorius cornu anterioris. N.c.p., nucleus proprius cornu posterioris. Prop.c., proprioceptor. Rd.d.viii, radix descendens nervi vestibularis. Rd.a., radix anterior. Rd.p., radix posterior. Rm.c., ramus communicans. Tr.l.v., tractus latero-ventralis. Tr.m.l., tractus medio-lateralis.

on the structure of the spinal cord. The results at which we had arrived independently agreed so closely that we have tried together to plan a scheme of the primary reflex arcs of the cord. In fig. 6 this scheme is reproduced. We started with the idea that the primary spinal reflex arcs subserve, in the first place, the more primitive spinal

reflexes. The primitive exteroceptive reflexes elicited from the skin are, in our opinion, the nociceptive withdrawal reflexes, of which the simple flexion reflex is the most common type. The primitive proprioceptive reflex initiated in the motor apparatus itself is tonus. The labyrinth, in as far as its impulses help to maintain tonus, we associate for well-known reasons with the proprioceptive system. The primary spinal reflex arcs are, we believe, homosegmental, at least in those cases in which the primitive segmental character of the sympathetic system is still preserved. When, however, the outflow of the sympathetic fibres from the central nervous system contracts and becomes confined to the thoraco-lumbar part of the cord, this primitive character of the primary reflex arc is of course modified. Assuming that the primary reflex arc in the lumbar region of the frog's spinal cord is still homosegmental, we reproduce in our scheme only those elements which appear in a sequence of cross-sections of a single spinal segment. The new fact incorporated in this scheme is represented by the nucleus intermedio-medialis. (Cajal [5], Bok. [3].) By the intermediation of the cells of this nucleus the stimuli reaching the cord by way of the posterior roots are distributed over the efferent sympathetic cells of the nucleus intermedio-lateralis and to the motor cells of the anterior horn, reaching first the efferent sympathetic cells and then the motor cells of the anterior horn. The nucleus intermedio-medialis is, therefore, the final common centre of the primary spinal reflex arcs.

In order that this scheme may not be misunderstood, we call attention to the fact that the more complicated combinations of movements, especially progression and active attitude, are initiated by stimuli emanating from centres lying above the medulla oblongata. The fibres connecting these centres with the spinal motor centres enter the antero-lateral tract above the level of the primary motor centres where they terminate. These fibres are present in large numbers, but have been omitted in the scheme as not pertaining to the primary spinal mechanism. For the same reason there have been omitted the labyrinthine fibres that enter the antero-lateral tract above the level of the second spinal nerve, as well as all intersegmental associative fibres.

On the basis of this scheme we may now say more precisely what is meant by the word "local" in the term "local shock." On dividing the rami communicantes it is clear that shock affects, in the first place, the sympathetic efferent section of the primary spinal reflex arc, i.e.,

the nucleus intermedio-lateralis, and that when it spreads it reaches the nucleus intermedio-medialis. Similarly division of the posterior roots causes, in the first place, shock in the afferent section of the primary spinal reflex arc, i.e., in the nucleus proprius cornu posterioris; then the shock extends to the nucleus intermedio-medialis. The fact that shock affects the nucleus intermedio-medialis after section of the rami communicantes, as well as on section of the posterior roots, is the reason of the close correspondence in the state of the animal immediately after those two operations.

In conclusion, I have to thank my colleague, Professor Zwaardemaker, who in the most courteous manner placed his laboratory at my disposal.

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THE CENTRAL CONNECTIONS OF THE VESTIBULAR NUCLEI WITH THE CORPUS STRIATUM, AND THEIR SIGNIFICANCE FOR OCULAR MOVEMENTS AND FOR LOCOMOTION.

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THE main facts about the cerebrotugal tracts have been known for some considerable time, but it is only of late that even a preliminary knowledge of the central ascending connections of the cerebral sensory nerves have been attained.

Monakow, Cajal, van Gehuchten, Probst, Horsley, O. and C. Vogt, and Sachs have pointed out the great importance of the thalamic nuclei as central stations for all corticopetal connections.

Wallenberg, Spitzer, van Gehuchten, and Hoesel were among the first to investigate the central connections of the more important sensory nerves—the N. trigeminus and N. vestibularis. As a result of these investigations a certain amount of light was thrown on the cerebropetal tracts of the N. trigeminus, but very little was learned about the central connections of the N. vestibularis. It is a curious fact that although physiological and anatomical data indicate the importance of these central connections, practically nothing was for long known about them. This is evident in Horsley's Boyle lecture of 1905, since in this lecture support is given to Mill's supposition that vestibular ascending connections arrive in the temporal convolutions. This view is, however, not accepted by Winkler, Kappers and Brouwer, who regard the lateral fillet as the pathway, or one of the pathways, for ascending vestibular stimuli to the higher cerebral centres. In 1914, [9], proof was forthcoming that the vestibular central connections pass upwards almost entirely in the posterior longitudinal bundle. A few pass from the nuclei tecti, where the cerebellar root of the vestibular nerve terminates, through the anterior cerebellar peduncle. Another tract may pass upwards from the nucleus ventralis raphé, but this is doubtful.

These few facts represented the sum of our knowledge of the central connections of the vestibular nuclei, and yet these connections are of the first importance for ocular movements, for equilibrium and for locomotion. Free locomotion and ocular movements in more than one plane are first seen in the lower vertebrates coincidentally with the

appearance of a vestibular organ, or some comparable apparatus, and with the development of a primitive corpus striatum.

From the clinical aspect, the regular appearance of typical disturbances of equilibrium of the cerebellar type in cases of tumour of the brain, and the presence of nystagmus and conjugate deviation of the eyeballs in variously localized lesions of the cerebral axis, indicate unmistakably the existence of ascending tracts from the vestibular nuclei.

The extraordinary importance of the subject and our very meagre information seemed to me sufficient excuse for this paper describing my work on the central connections of the vestibular nuclei, even if it be as yet incomplete.

Before passing to a description of my work and its results I would point out that the anatomical-physiological methods adopted by me in this and in earlier work [9] are not yet recognized by other workers.

Observations were first made by a series of lesions in the brain-stem of the cat. It was found that only lesions of the posterior longitudinal bundle resulted in forced movements in the horizontal plane (circus movement and conjugate deviation of head and eyes) and in the frontal plane (rolling movements and squint deviation of the eyes). Lesions elsewhere in the brain-stem were never followed by these types of deviation or movement.

Further, it was found that the direction of those forced movements was reversed when the lesion (hemisection) reached the region of the posterior commissure, and the nucleus commissuræ posterioris and nucleus interstitialis. From my observations these nuclei form the termini for the ascending fibres of the posterior longitudinal bundle after they have crossed in the posterior commissure. From these nuclei also originate the two descending tracts in the posterior longitudinal bundle (tr. commissuro-medullaris and tr. interstitio-spinalis or Boyce's tract).

It was also observed that a unilateral lesion of structures oral to these nuclei, involving the strands of fibres between them and the globus pallidus, was also followed by forced movements in the reversed direction. This phenomenon seems to be best interpreted by the assumption that nervous continuity exists between the two commissural nuclei and the globus pallidus.

In connection with this last observation, it is interesting to note that C. and O. Vogt [21], whose work is on purely anatomical lines, have also come to this conclusion, that a direct nervous connection exists between the commissural nuclei of the one side and the globus pallidus of the other. This partial anatomical confirmation of facts obtained by me with the anatomo-physiological method seems to be a valuable

argument in its favour, and goes far to justify its adoption in attempting to trace the ascending vestibular tracts.

In an earlier paper [9] I pointed out that within the nuclear complex of the N. vestibularis in quadrupeds a very high degree of differentiation of function is attained. On each side of the median line are two nuclei, lesions of which cause circus movements but in different directions. Lesion of one of the nuclei produces circus movements to the same side, while lesion of the other is followed by circus movements to the other side. Injury of the tracts ascending from these nuclei to join the mesial part of the posterior longitudinal bundle also results in similar forced movements. Further, on each side of the median line lie two nuclei, injury of which causes rolling movements. These nuclei show the same differentiation as those associated with the circus movements, since a lesion of one results in the rolling movements being directed towards the affected side, while injury on the other is associated with rolling movements directed towards the opposite side. The ascending fibres from these two nuclei are localized in the lateral wing of the posterior longitudinal bundle.

It is important to note that in a cross section involving the whole of one longitudinal bundle, including as it does the fibres concerned with circus movements to both sides, the result is circus movement to the intact side, rolling movement to the affected side. If, however, the lesion is situated oral to the posterior commissure the circus movements and rolling movements are conversely directed towards the affected and the intact sides.

It is found in monkeys, cats and birds, that a lesion involving the nuclei tecti and their ascending fibres in the superior cerebellar peduncle is followed by the falling backward of the animal, or at least a conjugate deviation of the eyeballs upward. On the other hand if the lesion involves the grey matter near the raphé of the medulla (nuclei of the raphé) and the medial nuclei of the pons the result is a distinct tendency to fall forwards. Further, a lesion in this region of the human brain appears to be associated equally with nystagmus and a forced position of the eyeballs in the vertical plane.

Before passing to the main subject matter of this paper I would recall my earlier work of 1907 [8] where I demonstrated that the nucleus tecti receives direct as well as indirect fibres from the vestibular nerve. This was subsequently confirmed by de Villaverde [20]. These data on the anatomical, physiological relations of the vestibular nerve may form a basis for further investigation, for there is, as far as the Marchis-stain goes, evidence that no other ascending vesti-

bular pathways exist. Careful workers consider the lateral fillet as a possible pathway for secondary vestibular tracts. This view they regard as being phylogenetically sound.

In the evidence which I offer for the solution of the problem I shall confine myself to one case in which the experiment may be regarded as crucial.

The experiment, which was performed on a cat, was carried out as follows: A protected needle, as devised by Probst, was used to pierce the medulla. This was introduced from behind on the right side and manipulated so that the vestibular region was completely destroyed (figs. 1 and 2). The needle pierced the lateral fillet at the level of the mesencephalon. On examination it was found that all the tracts described by me as secondary vestibular tracts were degenerated (fig. 3). The lateral fillet was quite free from any degenerative change up to the point where the needle pierced it (fig. 4). From this point marked degeneration extended right up to the end station in the thalamus (fig. 5). I repeated this experiment several times with the same result, viz., no degenerative changes occur in the lateral fillet from injury of the vestibular nuclei.

The result of these experiments is, in my opinion, sufficient to justify the conclusion that the fillet contains neither primary nor secondary vestibular fibres.

The next point for investigation is whether the physiological method used in the anatomical analysis of the primary and secondary vestibular connections will serve equally well for the elucidation of the tertiary vestibular connections. By tertiary vestibular connections are meant those tracts which connect the supra-nuclear centres (i.e., the nucleus commissuræ posterioris and the nucleus interstitialis) near the posterior commissure with the prosencephalon.

Theoretically no objection can be raised to the method, but the fact must be remembered that the physiological effect of a lesion of the ascending vestibular connections diminishes markedly the farther it lies from the entrance of the vestibular nerve. A second point is that the resulting forced movements vary in degree in different animals. Thus in rabbits they are very vigorous, but are much less when the same experiment is performed on animals higher in the scale. Thus in man a lesion of the ascending tracts causes only a forced position of the eyes, or a still less impressive phenomenon, a tendency to conjugate deviation ("Blickparese" of the Germans), or a tendency to fall or walk to one side when the eyes are closed.

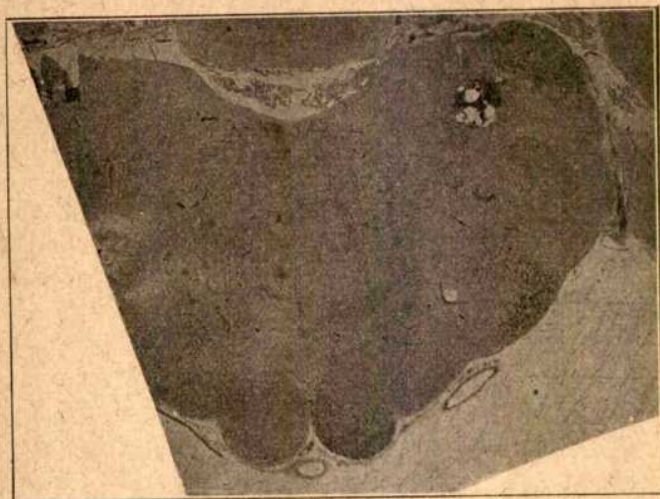


Fig. 1.

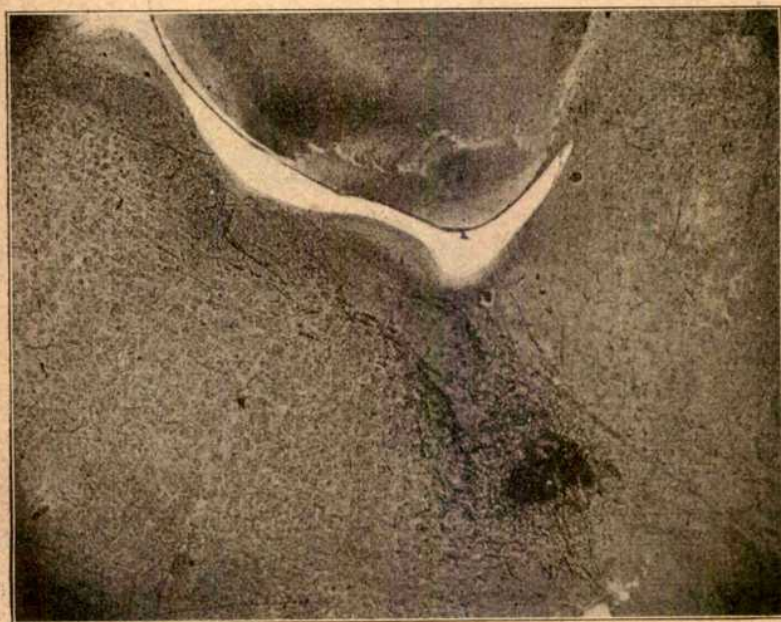


Fig. 2.

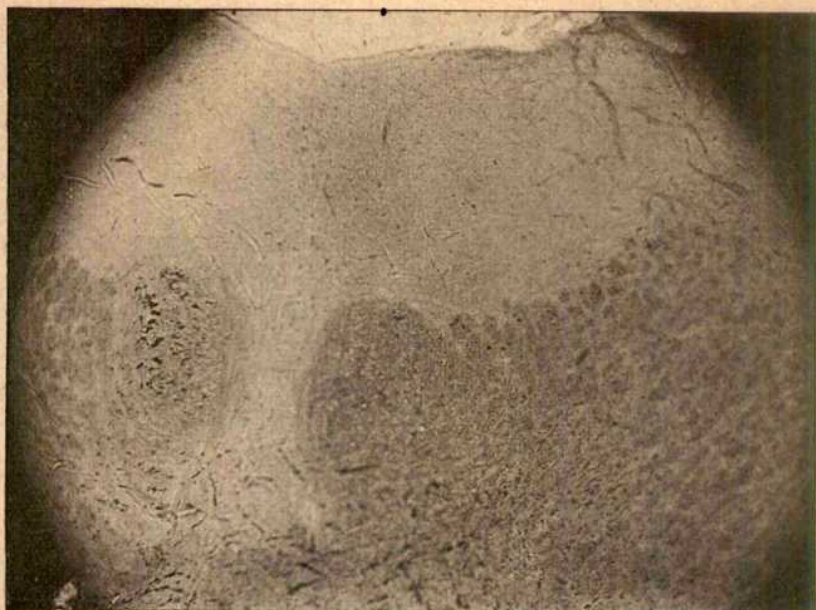


Fig. 3.



Fig. 4.



Fig. 5.

FIGS. 1-5.—Cat. Lesion of the vestibular nuclei. Ascending degeneration in the posterior longitudinal bundle only. Note absence of degeneration in the lateral fillet.

Again, in quadrupeds section of the vestibular nerve causes, as a rule, violent rolling movements to the side of the lesion, whereas a lesion of the ascending connections of the vestibular nuclei in the midbrain (posterior longitudinal bundles) is followed merely by a tendency to fall towards the affected side. In the human subject even this may not occur, but there is a tendency to lie in bed on the affected side, or to lean over to that side when sitting up.

It is, therefore, not remarkable that the result of severance of the tracts connecting the supranuclear centre (nucleus interstitialis) with the prosencephalon should be only a slight tendency to fall towards the normal side. It must be remembered, however, that this symptom although slight is very constant. Further, after a lesion in the prosencephalon in quadrupeds, the circus movements which result are neither so marked nor so persistent as those seen after section of the mesial portion of the posterior longitudinal bundle. Sometimes this circus movement to the side of the lesion may last a few days only, especially if the lesion be slight, but there may be a tendency for some time for deviation of the head and eyes towards the lesion. In monkeys and in man regular circus movements never result, but there is a distinct tendency to look towards the lesion. If the subject be blindfolded and told to march there will be seen a clear tendency to deviate from the straight line.

Regarding forced movements in the frontal plane, after prosencephalic lesions in quadrupeds there is a tendency to fall towards the normal side, accompanied by a deviation of the eyeballs known as the "Magendie-Hertwig squint." In man both these symptoms must be looked for very carefully, or they are completely missed. Careful observation is necessary to detect forced movements in the sagittal plane (forwards and backwards) in quadrupeds, while in man their observation requires special attention. Consequently the physiological-anatomical analysis of the tertiary vestibular connections has to be carried out with the utmost circumspection and critical care.

When we take into consideration how little is known of the physiology of the corpus striatum it is not surprising that its significance as a vestibular end-station has only recently been recognized. Remarks in the literature indicate that attention has been attracted to the corpus striatum in cases of conjugate deviation and forced movements. Prevost [12] calls attention to the fact that when in apoplexy the apoplectic area involves the corpus striatum, conjugate deviation of the head and eyes towards the side of the lesion results. Prus [14] notes that when

certain parts of the corpus striatum are stimulated electrically either pleurothotonus or elevation of the head results. Sachs [17] also records stimulation experiments of the same nature. Bechterew [1], who must be regarded as a pioneer in this work, records observations made by him of forced movements in dogs after lesions involving the base of the forebrain, and postulates the presence of vestibular centres in this region, although he does not mention the corpus striatum.

In experiments carried out by me on cats I found that lesions involving the region of the hypothalamus, the lamina medullaris ventralis and the globus pallidus were followed by circus movements to the side of the lesion and rolling movements to the normal side. Lesions involving other parts, as the anterior and median thalamic nuclei, or the anterior corpora quadrigemina, corpus geniculatum and corpus callosum, never gave rise to forced movements of any description.

The difficulties attending anatomical investigation of this region are very great. Dejerine and Horsley with their co-workers rendered valuable assistance to the investigation of nerve tracts by their application of the Marchi method. At the same time when an effort is made to extend the older physiological work of Majendie, Schiff, Probst and others, the difficulties, which of necessity beset so delicate an investigation, at once become apparent. The physiology of such regions as the red nucleus, the posterior commissure, the hypothalamus, the palæostriatum (globus pallidus, nucleus accumbens, area parolfactoria) and the neo-striatum (putamen and nucleus caudatus), is still a matter of conjecture. It can readily be understood how extremely difficult it is to produce sharply localized lesions in these regions. The formation of a thrombus may throw out of action a much larger area than is desired, and the direction or shape of the thrombus plays an important part. At the present time one cannot eliminate the element of chance from such experiments, but out of a series a few useful results may be obtained.

I now propose to discuss a series of sections prepared from the brains of a rabbit and a cat. The sections from the rabbit were prepared in the Central Brain Institute and were stained by the Weigert-Pal and van Gieson methods. The sections from the cat were stained by the Marchi method.

In both cases the posterior commissure was pierced by a needle (rabbit, fig. 9; cat, figs. 15 and 16) and the grey matter in front and on the mesial side of the red nucleus (region of the nucleus interstitialis)

was divided. In the cat the central grey matter of the aqueduct and the nuclei of the posterior commissure (Darkschewitchi) were also injured. The rolling movements which resulted in both cases appeared immediately after the operation, diminished after a few days, finally showing themselves only in a persistent tendency to fall towards and to lie on the normal side. Circus movements to the side of the lesion resulted only in the case of the cat and persisted for a few days only.

In the case of the rabbit, which survived for six months after operation, careful observation failed to discover any tendency to turn to one side more than another; it was highly probable, therefore, that Darkschewitchi's nucleus, which is associated with circus movements, escaped injury. Forced movements in the antero-posterior plane were seen in the cat only, and appeared as stepping and staggering movements. They were only present for the first few days after operation, and were probably due to lesion of the nuclei near the middle line.

The forced position of the eyes in both animals was that which usually accompanies the phenomenon of rolling movements to the right [5]. Both eyeballs were rotated round the visual axis towards the right side, the right eye being directed downwards, the left upwards.

It is interesting to note that both animals appeared to be blind immediately after operation, probably owing to the cross-section through the dorsal division of the posterior commissure. Later this passed off but hemianopsia towards the right persisted in both.

Microscopical examination of the brain and spinal cord of the cat showed the extent of the injury to be as follows.

The lesion in the middle line extended so far back that both bundles of Monakow were severed at their crossing, and they were consequently degenerated down to the lower segments of the cord. Both pyramidal tracts showed degeneration; the left was injured in the motor cortex as a result of the primary lesion, and also where the needle after piercing the midbrain reached the pes pedunculi.

The primary and secondary degenerations found in the posterior longitudinal bundles and the posterior commissure, with its nuclei and their connections, are particularly important. As these degenerations are for the most part identical in the rabbit and the cat, the fact that the Weigert-Pal and van Gieson methods were used in the one case and the Marchi method in the other makes the physiological and anatomical comparison of the two series more interesting.

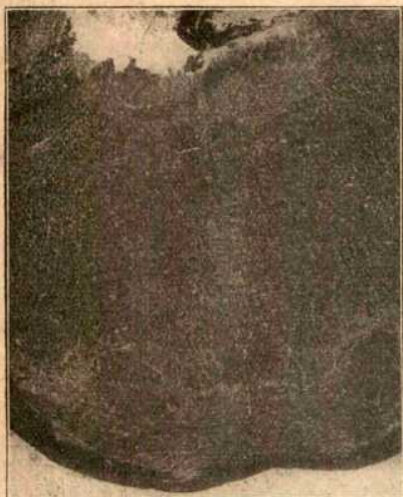


Fig. 6.



Fig. 7.



Fig. 8.



Fig. 9.

Examination showed complete division of the posterior commissure. This is a lesion rarely described in literature, but was noted by Probst [13], Buzzard and Collier [2]. In the rabbit the secondary ascending vestibular tracts in the posterior longitudinal bundles were divided. In

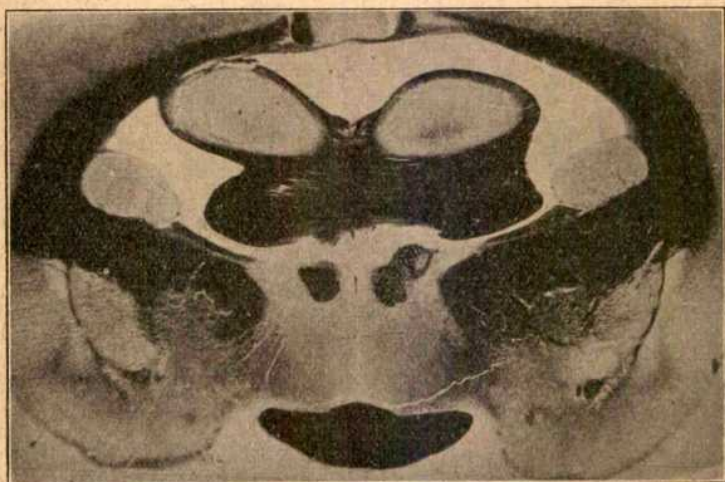


Fig. 10.

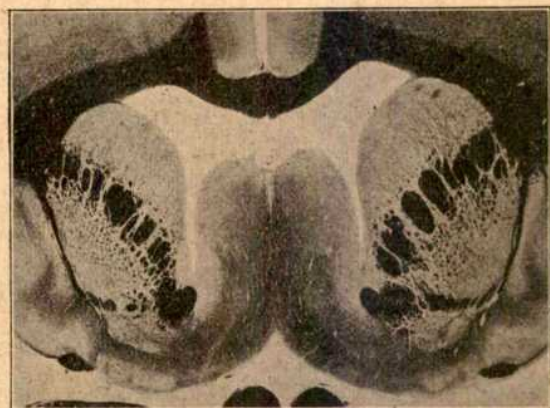


Fig. 11.

FIGS. 6-11.—Rabbit. Lesion of the commissural nuclei on the left side. Descending degeneration of the mesial part of the left posterior longitudinal bundle, and of the lateral horn of the right posterior longitudinal bundle. The left globus pallidus is diminished in size.

the cat the lesion was more limited to the middle line. It was found that on the left side (the side of the lesion) both the commissuro-medullaris and the interstitio-spinalis (Boyce's tract) tracts were degenerated

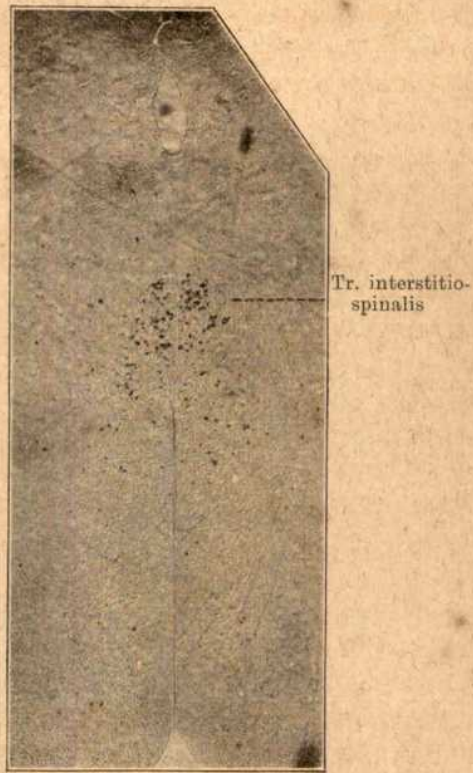


Fig. 12.

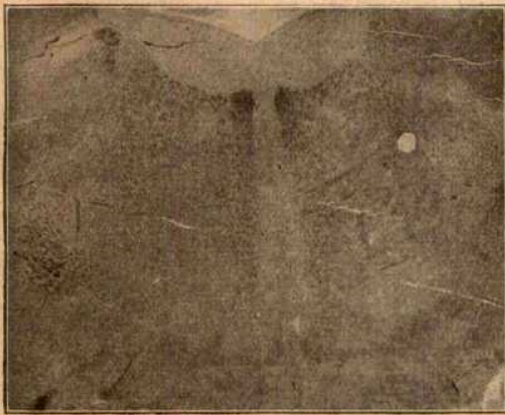


Fig. 13.

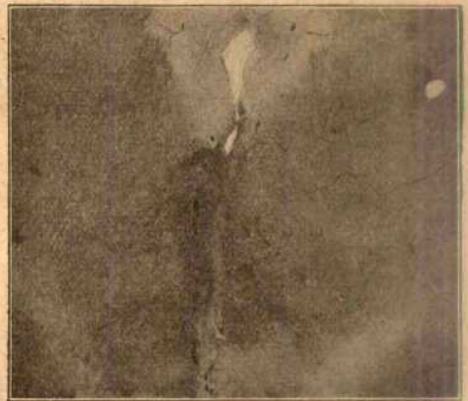


Fig. 14.

(figs. 12, 13). The lesion crossed the middle line, injuring the right posterior longitudinal bundle, and the interstitio-spinalis tract of this side also showed degeneration (fig. 14).

In the rabbit the left posterior longitudinal bundle in the medulla oblongata, particularly in its median portion, was less prominent than on the right side (fig. 6). In the pontine region this difference was less noticeable. It appears probable, therefore, that in this case the nucleus commissuræ posterioris suffered less injury, and as a result the commissuro-medullaris tract.

The most important point in these two experiments is that they afford an opportunity for seeing the orally situated structures with which the mesencephalic nuclei are connected.

In the rabbit, where rolling movements alone were seen, the lesion of the commissural structures was more limited. With the Weigert-Pal stain the corpus striatum presents the same picture as that described by Monakow in a rabbit [7]. These histological changes are as follows: The entire left globus pallidus, less so the putamen, but not the nucleus caudatus, show a decidedly atrophic appearance, compared with the normal side. Forel's field on the affected side is also rather thin, while the lamina medullaris externa thalami is not at all prominent (figs. 9, 10).

In the cat (241) the Marchi stain demonstrates the course of the striopetal fibres from the commissural nuclei. In following the fibres from the commissural region it is seen that the crus cerebelli ad thalamum of the left (side of lesion) is the more prominent; the majority of its fibres disappear orally in the neighbourhood of the lamina dorsalis thalami (fig. 16). From the capsule of the red nucleus a number of degenerated fibres pass at first ventrally, then laterally, in the direction of Forel's field. The lamina medullaris externa is thickly dotted with fine black spots (fig. 17). It is certain that a number of degenerated fibres are lost in the body of Luys's nucleus, in Forel's field, and probably also in the middle and anterior thalamic nuclei. The majority, however, of these ascending fibres, which are in all probability mostly vestibular, disappear in the direction of the globus pallidus (fig. 18). The external capsule of the putamen, especially in its anterior part, is markedly degenerated. In the putamen proper there is very little evidence of degenerated fibres. Fig. 18 shows the capsule on the right side, where, however, the degeneration is not nearly so great as on the left side, where the commissural nuclei are completely destroyed. It was impossible to obtain a satisfactory photograph of the left side.



Fig. 15.



Fig. 16.



Fig. 17.

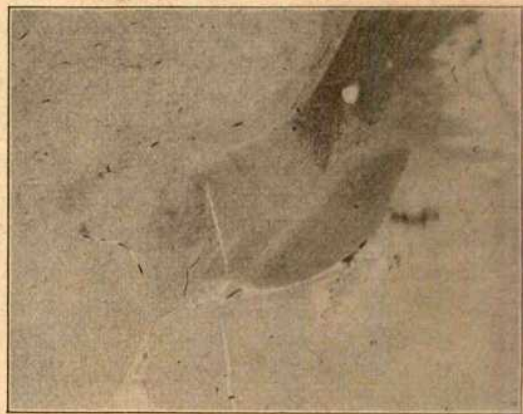


Fig. 18.

FIGS. 12-18. — Cat. Lesions of the commissural nuclei, mainly of the left side. Descending degeneration of the interstitio-spinal tracts, and less so of the commissuro spinal tracts. Ascending degeneration towards the globi pallidi, mainly on the left side.

These facts confirm results obtained by me in experimental work on cats. In some of these animals the globus pallidus itself was injured, or the lamina medullaris externa was severed. In such cases histological examination shows degeneration of fibres to the commissural nuclei and red nucleus on the one side, and to the globus pallidus on the other. Further, they agree with the anatomical observations of Wilson [23], who with the use of Clarke's apparatus demonstrated the existence of fibres passing from the putamen to the region of the globus pallidus and thence towards the capsule of the red nucleus.

I therefore conclude from this evidence that the commissural nuclei are in neuronal continuity with the globus pallidus of the same side. This connection consists of at least two neurons between the globus pallidus and the commissural nuclei, whereas in the reverse direction but one neuron exists.

These results may appear unexpected to the physiologist and the clinician, but if the work of Bechterew, Probst and Dejerine [3] is carefully considered, it is evident that considerable support for the results is forthcoming.

In the last section I called attention to the agreement in many points between my work and that of Wilson. In certain particulars, however, we differ. Wilson speaks of connections from the region of the globus pallidus passing to the region of the red nucleus. In all my experiments the red nuclei were intact, and it is extremely probable that the bulk of the globus pallidus connections do not reach the red nucleus at all, but pass to the two nuclei situated anteriorly and medially to it. It is probable that this investigator did not realize the existence of the nuclei commissuræ posterioris and interstitialis and their descending tracts in the posterior longitudinal bundle.

It is important when considering results obtained by other workers to remember that the application of the nomenclature differs somewhat in different countries. The English workers apply the term "ansa lenticularis" to the whole of the mass of fibres lying between the commissural nuclei, the red nuclei and corpus striatum, and more particularly to those fibres which penetrate the internal capsule to join the globus pallidus. Monakow, Winkler, Potter, Dejerine and his school apply the name only to the fibres lying between the mesencephalic nuclei and the more anteriorly situated parts of the corpus striatum.

It is not my intention to discuss afresh in detail the physiological points as applied to the human subject raised in this and in my earlier

paper [9] in which an anatomical-physiological investigation of the posterior longitudinal bundle revealed only two descending tracts in its median part. One passes down from the nucleus commissuræ posterioris (tractus commissuro-medullaris) and is associated with circus movement and conjugate deviation of the eyes to the same side; the second tract passes down from the nucleus interstitialis (tractus interstitio-spinalis, Boyce's tract) and is associated with rolling movement and the development of the Majendie-Hertwig squint. In this paper (p. 418) I concluded thus: "If this symptom (tendency to fall to the right) is present where the disease is localized cephalad to the posterior commissure, then from experimental findings the lesion is to be localized in the optic thalamus or striate body on the left side." When this was written I had already made use of the direction of these forced movements for purposes of localization in brain disease, particularly for diagnoses of frontal diseases.

It is interesting to find that in war literature is the first, and I think, decisive confirmation for this solution of the localization problem. Gerstmann [4], writing in 1916, published six cases of unilateral lesion of the frontal brain. In all the cases there was a disturbance of equilibrium demonstrated as a falling to the healthy side. The writer of the paper was evidently unaware of my paper (1914), and therefore could not appreciate the confirmation given to my suppositions. I therefore regard this falling to the healthy side as an important diagnostic sign in disease of the frontal lobe, or, to state it more exactly, of involvement of the globus pallidus or its connections with the commissural nuclei. Further experimental as well as clinical evidence seems to show that only in lesions of the globus pallidus do lasting circus movements and conjugate deviation of the eyes to the side of the lesion or a tendency to fall over to the healthy side result. From this one must admit continuity of anatomical connections from the vestibular region upward through the brain-stem to the globus pallidus. It must be remembered that a lesion of the putamen alone causes these disturbances for a short time only.

SECTION II.

Pathological lesions in man comparable to the above experimental lesions in cats and rabbits are rare.

In the Brain Institute in this city I found nothing to correspond with them. My attention, however, was drawn to a series of sections of the brain of a case of Meer en Berg, where a thrombotic process had caused atrophy of a great part of the left hemisphere.

The cortex of the entire frontal and parietal region was reduced to a thin lamella in which no traces of the convolutions could be detected. The corpus callosum was atrophied. The left lateral ventricle was enormously distended. Of the left corpus striatum the nucleus lentiformis was completely absent, and no part of the left putamen could be considered normal, and only a small number of cells were found in the globus pallidus. As this case has been discussed for other purposes and drawings of sections of it published [19], I shall limit myself to a statement of those details which are of importance for the present research.

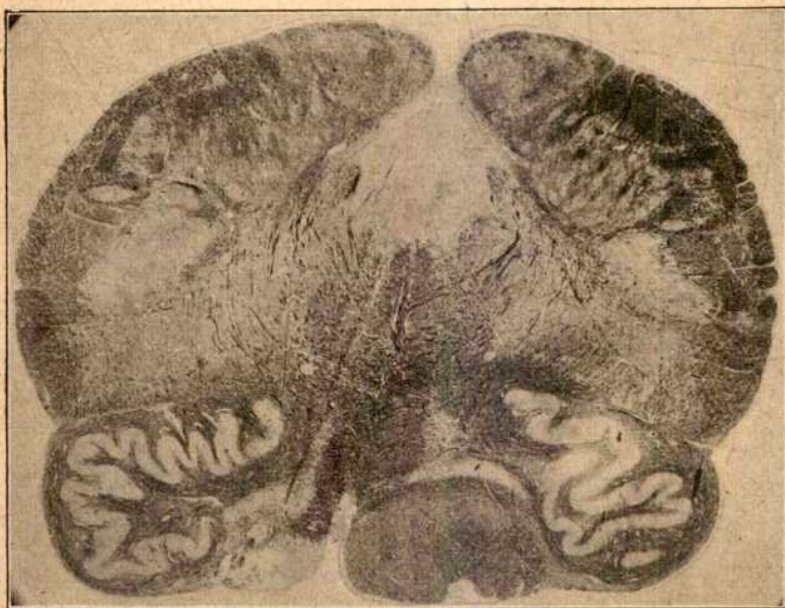


Fig. 19.

In the first place I would direct attention to the difference in size of the posterior longitudinal bundles, that on the side of the lesion being diminished (figs. 19, 20, 21, 22, 23). This difference in size must be explained by the interdependence of the globus pallidus and the homolateral nuclei (nucleus interstitialis and nucleus commissuræ posterioris), as has been shown experimentally in the rabbit. This being so, partial destruction of the globus pallidus is inevitably associated with atrophy of these nuclei and insufficient development of the homolateral fibres descending in the posterior longitudinal bundle [9].

The work of Edinger, Ramon y Cajal and my own unpublished observations on the constitution of the ventral part of the posterior commissure, would show that those nuclei receive afferent impulses from the heterolateral branch of the commissure, this being the continuation of

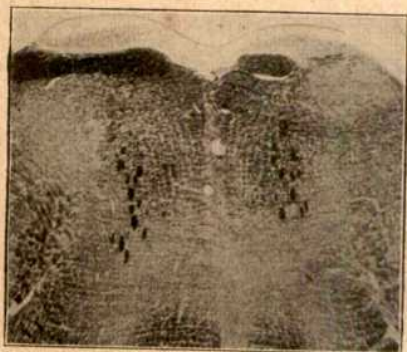


Fig. 20.

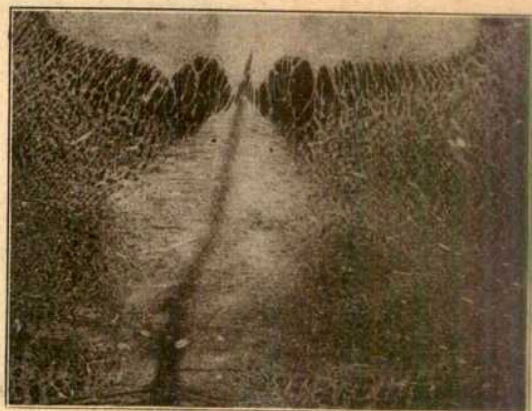


Fig. 21.

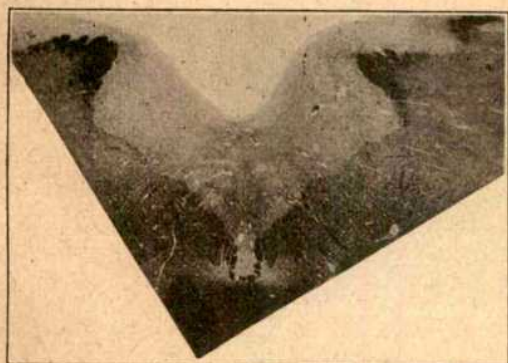


Fig. 22.

Note the fewer fibres in the mesial part of the left posterior longitudinal bundle.

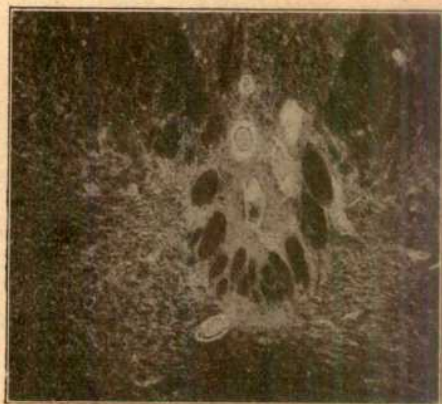


Fig. 23.

A portion of fig. 22 photographed under a higher magnification.

the lateral horn of the posterior longitudinal bundle. It is therefore not surprising to find in this case that the right arm of the commissure contained fewer fibres than the left (fig. 22).

This case is comparable with the experimental rabbit; in the rabbit

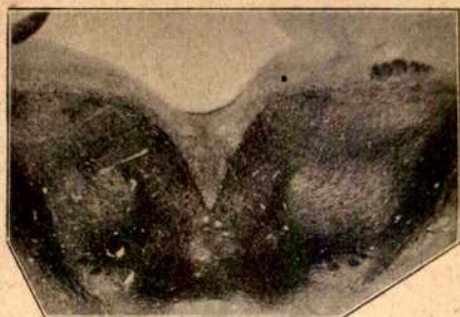


Fig. 24.

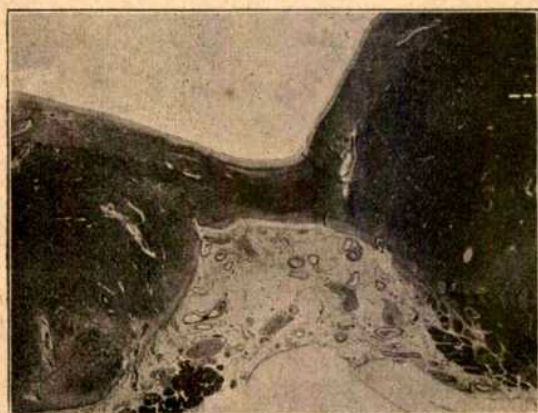


Fig. 25.

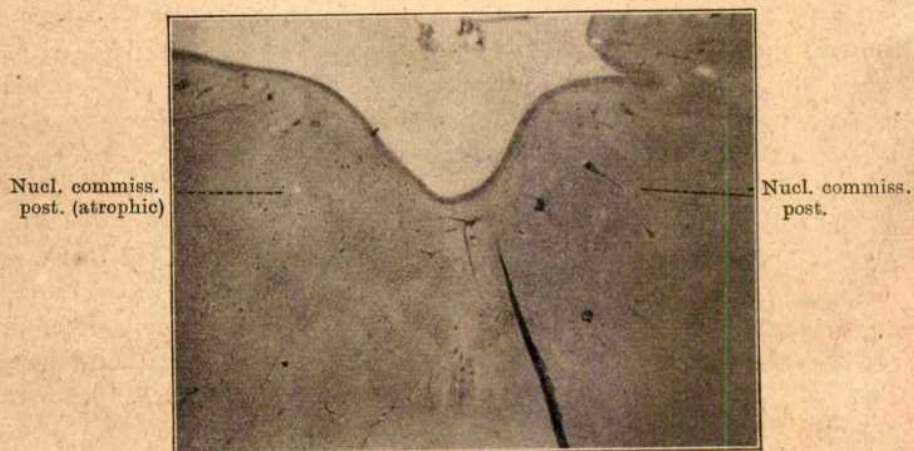


Fig. 26.

FIGS. 19-26.—Section of a human brain in which a destructive lesion of the left corpus striatum had occurred several years before death. The left nucleus commissuræ posterioris and nucleus interstitialis are atrophic. Poverty of fibres in the lateral horn of the right posterior longitudinal bundle, and in the corresponding part of the posterior commissure. In fig. 19 note the smallness of the left posterior longitudinal bundle owing to absence of the tr. interstitio-spinalis.

the lateral wing of the posterior longitudinal bundle on the side of the lesion involving the commissural nuclei was more voluminous than on the other side (fig. 6). In the human brain destruction of the left globus pallidus is also associated with a greater development of the lateral wing of the left posterior longitudinal bundle (fig. 21).

From these facts we must recognize a cerebropetal structural and functional continuity between the left corpus striatum, the right arm of the posterior commissure and the lateral wing of the right posterior longitudinal bundle. Further, it is also found that the left corpus striatum is cerebrofugally connected with the commissural nuclei, and by means of these with the descending fibres in the innermost part of the mesial segment of the left posterior longitudinal bundle.

Finally I would direct attention to the red nucleus.

When the series of sections are examined from below upwards it is found that these nuclei first appear in the same cross-section (fig. 24). It is probable, therefore, that the caudal parts at least of these nuclei are not dependent on the corpus striatum of the same or the other side.

In fig. 25 the frontal part of the right red nucleus is seen, but of the left there is no trace. It would, however, be premature to conclude that the frontal part of the red nucleus has a special relation to the homolateral corpus striatum, since the exact homology of those regions is unknown. The difference in the oral parts of the red nuclei might be due to the fact that in man the nucleus interstitialis is represented by the frontal part of the red nucleus.

From further experimental work I maintain the conclusions put forward in my former paper [9], that the nucleus commissuræ posterioris and the nucleus interstitialis represent superimposed vestibular nuclei. These nuclei receive their stimuli from the ascending elements of the crossed posterior longitudinal bundle via the posterior commissure. The descending fibres from them, the tractus commissuro-medullaris and the tractus interstitio-spinalis, are situated in the mesial division of the posterior longitudinal bundle. The descending fibres or tracts are concerned with locomotion in two planes (circus movement with conjugate deviation of head and eyes, and rolling movement with Hertwig-Majendie squint).

It must be admitted that for some reason a lesion of the ascending elements of this vestibulo-motor nerve chain prevails in its effects over lesions of the descending elements. This is shown by the fact that in a series of hemisections from the pons upwards the direction of the

forced movements changes as soon as the posterior commissure is reached. Further, the supra-nuclear centres are connected with the corpus striatum, or at least with the oral part of the globus pallidus. The direction of the forced movement does not change wherever the supra-nuclear section is made. If an animal with a lesion in this part survives sufficiently long some loss of fibres may be found in the mesial part of the posterior longitudinal bundle, and also in the wing of the posterior longitudinal bundle of the crossed side. This descending degeneration has been observed in the case of a patient of my own with recent destruction of the globus pallidus, and also in similar cases recorded by Dejerine and Roussy [16].

SECTION III.

My earlier work on this subject [9] indicated that the commissural nuclei (N. commissuræ posterioris and N. interstitialis) as well as the secondary, and perhaps tertiary, vestibular tracts which compose their afferent systems, are concerned exclusively with locomotion and conjugate deviation of the head and eyes in the horizontal and frontal planes. It is proposed to give here a short note on the fibres and nuclei which subserve forced movements in the sagittal plane, that is locomotion and conjugate deviation of the head and eyes upwards and downwards.

The nuclei and fibres which determine forced movements in the horizontal (circus movements) and frontal (rotation round the body axis) planes are situated symmetrically on either side of the middle line, one system co-ordinating the deviation or rotation to the right, the other to the left. Physiological and clinical data tend to show that entirely different nuclei and tracts determine vertical deviations. This is not surprising since the one set of movements—standing up, looking upwards, falling backwards, going backwards—is not the reflected image of the other set—stooping down, looking down, falling forward, going forward.

The upward and downward forced movements are never of the violent character seen in rabbits when the vestibular nerve has been injured. Further, they seem very easily compensated. During the first few days after operation on the cat (241) there was a tendency to recoil, to fall backward and to go backward, and a very slight pressure under the chin caused the animal to sit up. This form of forced movement in the sagittal plane invariably follows a lesion of the nucleus

tecti cerebelli in the cat and the pigeon. It is interesting to find that there is some clinical evidence on this point, similar forced movements occurring in cases of tumour of the cerebellum involving the nuclei tecti.

Wallenberg [22] working with pigeons found that after lesions of the superior cerebellar peduncle there was a tendency to retrogression, and thought that injury to some nucleus in this region was associated with the development of these movements. Marburg, Bing, and Ingvar also found that lesions of the spino-cerebellar tracts in animals were associated with disturbances of locomotion in the antero-posterior direction.

In 1907 I described the terminations of fibres of the vestibular nerve in the nucleus tecti. It seems highly probable that the nucleus tecti plays the same part in forced movement in the antero-posterior direction as Deiters' nucleus and the descending vestibular nucleus do in circus and rolling movements. The fact that the ventral and dorsal spino-cerebellar tracts terminate in the nuclei tecti seems to corroborate this view [10].

In a series of sections through the brain of the cat (241), already referred to, a tract of degenerated fibres is seen on both sides of the section lying on the inner side of the anterior cerebellar peduncle (fig. 13). The position of this tract is almost identical with the hook-like structure found by Russell [16] in dogs after a median incision between the nuclei tecti. This structure was also described by Thomas [18]. The difference between my case and the cases of Russell and Thomas is that in their cases the degeneration was cerebello-fugal while in mine it is cerebello-petal. This in no way serves as an argument against my view but is rather evidence in favour of it, since from the time of Held [5], who first drew attention to the fact, it has been more and more appreciated how frequently the ascending and descending secondary and tertiary vestibular pathways lie in the same areas.

At present we can only surmise which supra-mesencephalic nucleus receives these fibres, but probably it is situated ventrally to the posterior longitudinal bundle in or near the raphé. This suggestion is made from a study of the rabbit already described where the structures of the median line were intact, and where no trace of forced movements in the vertical plane occurred.

Physiological and clinical observations therefore tend to show that a lesion near the median line in the thalamic region will cause

staggering, and walking or falling backward, as do lesions of the prosencephalon if not situated too ventrally.

It seems justifiable to assume ascending connections similar to the tertiary striatal connections of the commissural nuclei, but passing to the palæostriatal nuclei septi.

Although experience has shown the utility of the physiological-anatomical method it must be understood that great care is necessary in its application. This is particularly so in attempting to demonstrate the tertiary vestibular connections where conclusions have to be drawn from transient and puzzling forced movements in the antero-posterior or sagittal plane. The forced movements in this plane are never violent even after lesions of the primary connections. It is also important to remember that the forced movements in the other planes (circus movement and rolling) decrease in strength the farther the lesion is from the primary vestibular fibres.

I may say in conclusion that I have carried out certain experiments and collected some clinical data on the position of the vestibular nuclei, the superimposed nuclei and their connections which may excite forced movements in the sagittal plane in the opposite direction to those already described, i.e., falling forward and locomotion forward. There is some evidence that the nucleus ventralis raphé is associated with this type of movement. In one experiment where the lesion involved the basal longitudinal bundle (Wallenberg) near its origin in the frontal brain the animal never sat up again in a natural manner, but held its head down. It may be surmised that the secondary tracts run up near the raphé and are situated somewhat ventrally. Further it seems probable that the tertiary ascending and descending fibres dealing therewith are to be found in the area of the basal longitudinal bundle of Wallenberg.

SUMMARY AND CONCLUSIONS.

(1) Persisting circus movements and lateral conjugate deviation of the head and eyes to the affected side, and a tendency to fall to the normal side after cerebral lesions, is due to injury of the oral part of the globus pallidus, or of its connections with the commissural nuclei (nucleus commissuræ posterioris and nucleus interstitialis). Hence the conclusion seems warranted that the tertiary vestibular tracts, lesions of which produce the same symptoms, terminate in this palæostriate centre.

The secondary vestibular tracts which ascend in the posterior longitudinal bundles cross the middle line by way of the posterior commissure before entering the nucleus commissuræ posterioris and nucleus interstitialis. In the diagram in my earlier paper [9] these ascending vestibular tracts were wrongly indicated as terminating in the commissural nuclei before crossing the middle line.

(2) It has not been possible to determine by the anatomical-physiological method the chains of neurons concerned in forced movements in the sagittal plane, i.e., recoil, retrogression, conjugate deviation of the head and eyes upwards; falling forwards and deviation of the eyes downwards. Experiments on cats, in which lesions of the nucleus tecti and of the superior cerebellar peduncle produce a tendency to recoil, recall the experiments on pigeons by Wallenberg, who assumed the existence of some such centre in or near to the superior cerebellar peduncle. Clinical and physiological observations lead us to suppose that structures exist in the mesencephalon, near the raphe and ventral to the posterior longitudinal bundle, lesions of which cause falling backwards and deviation of the eyes upwards. There is also experimental evidence that lesions of the palæo-striate nucleus septi (Kappers, de Vries) cause recoil and retrogression.

Near the middle line but more ventrally situated there are structures (? the basal longitudinal bundle of Bischoff and Edinger), lesions of which produce a tendency to fall forwards and deviation of the eyes downwards.

I have to acknowledge my indebtedness to Dr. Ariëns Kappers and Dr. Brouwer for their permission to make use of the material of the Central Brain Institute in Amsterdam, and to Mrs. Shaw Dunn for her kind help in correcting the English of this paper.

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Proceedings of the Section of Neurology of the Royal Society of Medicine.

CLINICAL MEETING, NOVEMBER 9, 1922.

Dr. WILFRED HARRIS, President, in the Chair.

(1) *A Case of Tremor of Rare Nature.*

By Dr. ANTHONY FEILING.

Gladys C., aged 10½, was brought to the hospital on account of involuntary movements of the left side of the body. She was a full-time child, a breech presentation and at birth had white asphyxia. Sat at 18 months, walked at 3 years. Has never had fits or other illnesses, except measles.

At the age of 9 months involuntary movements were noticed on the left side of the body, and weakness in holding up the head. During the last six months these movements have become worse and have extended to the other side of the body. At times her voice is very feeble. No history of any nervous disease in the family. The child is well grown and appears quite intelligent.

There is a slight weakness of the lower part of the right side of the face, while the tongue is deviated slightly to the left. The left arm is the seat of a rhythmical tremor, more marked in the proximal parts of the limb. The movements produce rotation of the arm at the shoulder, pronation and supination of the forearm, and flexion and extension of the fingers. The rate is about two to the second. Both arms are hypotonic.

Similar movements affect the trunk and the legs, though to a less extent. In the legs also the proximal muscles are involved to a greater extent than the distal. There is no actual paralysis, though the power of the left arm and leg is less than in the right limbs. The deep reflexes are present and the plantar responses are flexor.

(2) *Parkinsonian Syndrome associated with Right Hemiplegia, showing Peculiar Disturbances of Tone and Posture in the Limbs on the Hemiplegic Side.*

By Dr. DOUGLAS MCALPINE.

Patient, a female, aged 20, was quite well until April 18, 1919, when she developed a typical attack of encephalitis lethargica, complicated from the outset by a right hemiplegia. Her present condition developed gradually within a few months from onset.

The following is a brief summary of her present condition:—

Parkinsonian facies, smile and speech, with slight right hemiplegia and definite extensor response on right side; on left side doubtful extensor response. Power quite good all four limbs; no sensory disturbances.

At the proximal joints in all four limbs there is a slight resistance to both flexion and extension by passive movements, most marked in the lower limbs. If the fingers or wrist of the right hand be passively moved into any position, such position is maintained involuntarily. Right ankle when inverted, or everted remains in that position; this is not seen however in dorsal or plantar flexion at proximal joints, nor in the limbs on the left side.

Voluntary movements.—Extension at elbow is possible only when fingers are extended: with the fingers flexed there is always accompanying pronation; extension of fingers is possible only when patient voluntarily abducts the arm, flexes the elbow, pronates the forearm and flexes wrist, or when she extends the hyperpronated elbow. The postures of hand and wrist on voluntary movement of the limb tend to take one of four patterns:—

(1) Flexion of fingers and wrist. (2) Extension of fingers and thumb, wrist being flexed or slightly extended. (3) Extension of wrist and first phalanges, with flexion at interphalangeal joint and apposition of thumb. (4) Same position of fingers as in (2), but with flexion of the wrist and pronation of the forearm. The position of the elbow is variable.

All voluntary movements of the hand are carried out slowly and with difficulty. The phenomenon of tonic innervation is well seen in the right hand and wrist. If patient when grasping the observer's hand is then told to relax her grip she is unable to do so for a period varying between fifteen seconds and two minutes; she has to manœuvre her arm into the position described as necessary when extending the hand. This condition is not seen at the proximal joints, but occurs to a slight extent at the right ankle. There are no athetotic movements, nor motor apraxia. A flexion and sometimes an extension reflex (as described by Riddoch and Buzzard) is obtainable in both upper limbs when a nocuous stimulus is applied to either extensor or flexor aspect of arm.

On assuming the upright posture the right arm at once becomes extended at elbow, hyperpronated, flexed at wrist and deviated to the ulnar side, with fingers flexed into palm. As soon as right foot touches the ground it becomes powerfully inverted, with plantar flexion of foot and toes, but the hallux is dorsiflexed so that the pad of the toes alone touches the ground; at the same time there is extension of the knee. After half a minute or so the tonic spasm of the foot gradually relaxes and the right foot assumes its correct posture on the ground. On attempting to walk the right leg is overflexed at the hip and the whole leg goes into extensor spasm again, the attitude of the leg at this stage resembling that depicted in the goose-step of the German soldier. Gradually the right leg is lowered and toes approach the ground; then, as spasm relaxes, the heel is gradually lowered until it touches the ground, the weight meanwhile being transferred to right leg. As the right leg is carried forward the right arm, maintaining the posture described above with

palm turned outward, is powerfully retracted and abducted at shoulder, and as the patient transfers her weight on to the right leg the right arm comes forward again into line with the body.

Remarks.—In this case there is evidence of a moderately well developed condition of Parkinsonian rigidity associated with a slight right hemiplegia, and in all probability with some disturbance of the left pyramidal tract, as evidenced by the nature of this plantar response and the presence of a well-marked flexion reflex in the left upper limb; despite this bilateral pyramidal involvement there is an entire absence of pseudo-bulbar symptoms. There is no evidence that the phenomenon of tonic innervation depends on a lesion on a higher plane than the internal capsule, which, however, was the case in seven out of the nine cases collected by Wilson and Walshe. The condition seems to indicate lack of reciprocal inhibition of antagonists, so that one muscle group remains contracted despite volitional attempts to innervate the opposing group of muscles. In this case apparently the same phenomenon is present both on voluntary and on passive movement, and in the maintenance of a posture of right hand brought about by the observer; therefore no separation is possible between the phenomena occurring on voluntary and involuntary movement. It seems certain that in this case the condition of tonic innervation can be explained by a central lesion resulting in a disturbance of reflex tonus. The posture which develops in the limbs on the right side on standing or attempting to walk is clearly determined by the assumption of the upright position, and resembles closely the antigravity posture as described by Sherrington in the decerebrate animal.

I am indebted to Dr. Campbell Thomson for permission to show this case.

Dr. RIDDOCH, referring to the flexion reflexes of the upper limbs, said they were similar to those observed by Buzzard and himself in hemiplegia due to cerebral and spinal lesions. In this case there can be no doubt of the existence of a right-sided hemiplegia, and there is evidence that the left pyramidal tract has suffered too, in the indefinite type of the plantar reflex on this side. The tonic state of the muscles on the right side of the body, the "lead-pipe rigidity" of the limbs, and the persistent maintenance of postures, differs from that seen in both paralysis agitans and post-encephalitic lesions. The rigidity suggests that it might be the result of a combined hemiplegic hypertonicity and Parkinsonian rigidity. The postures of both the upper and lower limbs are not those usually observed in simple lesions of the pyramidal system. He emphasized the remarkable feature that the patient can open her hand only on supinating the arm, and that the whole limb extends when she closes her fingers. Similarly in advancing the leg the whole limb extends, and the ankle dorsiflexes only a considerable time later.

The PRESIDENT asked whether the present symptoms were the immediate sequel to the attack of encephalitis, or whether they had been progressive.

Dr. MCALPINE replying said that there was no interval between the acute symptoms of encephalitis and the symptoms which the patient now presents; these have been progressive. He was unable to accept Dr. Riddoch's suggestion

that the hypertonicity is due to the association of a hemiplegic and Parkinsonian rigidity.

(3) *A Form of Juvenile Amaurotic Idiocy.*

By Dr. GEORGE RIDDOCH.

The patient, aged 10, was the child of Jewish parents, who were also first cousins. A brother aged 13, and a sister aged 8, are both alive and well. Birth was normal and the child was breast-fed until 18 months of age. He walked at 9 months and used simple words at 1 year. Development was normal until 4 years of age when the legs became weak. At 6 the upper limbs were also affected and obvious symptoms of mental deterioration set in, the child becoming dull and apathetic, with occasional outbursts of screaming and destructiveness. At the age of 8 years vision was noticed to be affected, and a year later there was complete paralysis of all limbs, curious myoclonic movements, over-reaction to loud noises, blindness and complete idiocy. The child also became subject to epileptiform fits. Any loud noise was liable to evoke irregular purposeless movements. The child has wasted considerably.

Present condition.—Complete dementia, blindness and spastic paralysis of upper limbs in flexion and lower limbs in extension. Lies on his back with head to one side and saliva dribbling from his open mouth. Quick involuntary movements, especially of upper limbs, occur frequently. These myoclonic movements can be evoked by the slightest tap on any part of the body, and sometimes by a loud noise. They are often bilateral and symmetrical and are then accompanied by movements of the head and face, contraction of the muscles of the trunk and a grunting noise. All tendon reflexes are much increased and the plantar response is extensor on both sides.

Ophthalmoscopic examination reveals advanced optic atrophy and much pigmentary degeneration of the retina; there is a large mass of pigmentary change near the left macula. No cherry-red spot at the macula. The Wassermann reaction of the blood was reported as being doubtfully positive.

He discussed the relation of this case to the Waren Tay-Sachs type of amaurotic family idiocy, which is limited to the Jewish race, and to the juvenile forms of this disease which have been described by Batten and Mayou and by others.

The PRESIDENT said he had found it difficult to get a satisfactory view of the fundi, but that such changes as he had seen resembled those of retinitis pigmentosa.

Dr. GORDON HOLMES pointed out that this case differs in many of its present symptoms from the typical cases of infantile and of juvenile amaurotic idiocy. The term idiocy should not, in fact, be applied to such cases, since the mental state of the patient was apparently normal till 5 or 6 years of age. The most striking difference from the Spielmeier and Batten-Mayou groups is that in this patient there are, in addition to optic and retinal atrophy, large irregular patches of pigment in the retinae which resemble those due to

syphilitic retino-choroiditis. He was consequently not surprised that on one occasion the Wassermann reaction was positive or doubtful. Further, the pigmentary changes are grosser and more widely scattered over the fundus than in the Batten-Mayou group. In many of these cases the retinal degeneration belongs to, or resembles, the retinitis pigmentosa type, but the fundus changes he saw were not characteristic of this condition. There were unquestionably many forms of progressive dementia and paralysis associated with retinal degeneration, each rigidly typical for the several numbers of the family it affects, but differing in many respects from family to family.

Dr. PARKES WEBER suggested the possibility that the condition was one of juvenile general paralysis; the same type of spasmodic movements is not uncommon in this disease, and similar fundus changes are occasionally met with.

Dr. FEILING had also observed similar ocular changes in syphilitic conditions; he had recently seen them in a patient with tabes dorsalis.

Dr. RIDDOCH in replying admitted that the symptoms differed in many respects from those seen in the Batten-Mayou and Spielmeyer groups, and he must admit that similar retinal changes are found in both retinitis pigmentosa and in syphilitic conditions, but he could not see any justification for the suggestion that his case may be merely one of juvenile general paralysis.

(4) *A Specimen showing Endothelioma Cerebri in an Unusual Situation.*

By Dr. J. P. MARTIN.

Patient was admitted to the National Hospital under the care of Dr. Taylor, April 18, 1922, and died May 20. For three years he suffered with pins and needles in the third, fourth and fifth fingers of the left hand; this feeling was not present constantly and usually occurred in the morning. It spread slowly up the left arm, and he became unable to grasp objects with the left hand. Towards the end of 1920 the right arm was affected in the same way, but in it the paræsthesiæ spread from above downwards.

In January, 1921, he was admitted to St. Thomas's Hospital; his legs had been shaky but were still strong and did not cause any disability in walking; after lying in bed for four days he became completely paralysed. He gradually improved and was discharged three months later.

About July, 1921, he began to suffer from attacks of breathlessness. He was re-admitted to hospital, and again became weaker while lying in bed. About October, 1921, he became unable to feed himself or to use his arms. He never had dysuria or pain. On about a dozen occasions in three months before his admission to the National Hospital he had seen double.

On admission very helpless, with cyanosis of face and lips, and occasional attacks of breathlessness. A few nystagmoid jerks developed on extreme deviation of the eyes to either side, and there was slight left facial weakness.

There was nowhere loss to painful, tactile or thermal stimuli, but the appreciation of vibration was absent in both arms and both legs. The sense

of position was lost in the right hand and arm and in both feet, and impaired in the left hand. There was complete astereognosis.

Patient could not raise his head from the pillow, but could turn it from side to side. When he was sitting in a chair his head fell forwards. Both upper limbs were quite powerless, they lay slightly flexed at the elbows and wrists, with the fingers half flexed. There was no spasticity and no wasting or fibrillation of the muscles. The lower limbs lay at rest in full extension. The amount of power varied from time to time: after he had been lying down he was usually unable to make any movement, but after sitting up for a time he could make movements of fair power at all joints.

All the arm-jerks were brisk, the knee-jerks exaggerated, ankle-jerks present with clonus, the abdominal reflexes absent, and the plantar responses both extensor. There was defective control over both anal and vesical sphincters.

The Wassermann reaction was negative, and the electrical reactions of the muscles were normal. X-rays showed no spinal lesion.

Patient died of hypostatic pneumonia.

Autopsy.—The tumour, which weighs 32.5 grm., is pear-shaped and firm in consistence. It fills and distends the cisterna magna, lying between the arachnoid and the pia mater. A small knob on its upper and posterior surface compresses the right lobe of the cerebellum. It lies against the foramen of Magendie, but has caused little hydrocephalus as the foramina of Luschka are unusually wide. The posterior surface of the medulla, from the tip of the calamus scriptorius downwards, is hollowed out by its pressure. The pressure affects particularly the cuneate and gracile nuclei, the restiform bodies being only compressed at their posterior borders. At the lower end of the medulla the tumour passes to the right of the mid-line so that the right dorso-lateral surface of the first cervical segment is compressed. The cord at this level is softened. Microscopical sections show the tumour to be a typical fibrous meningeal endothelioma.

(5) *Case of Sclerodermia.*

By Dr. MARTIN.

In March 1921, patient had an illness said to be influenza. In May she had difficulty in kneeling on account of pain in the thighs and back. In November she began to experience stiffness after standing for a short time. Menstrual periods have been irregular since January 1921. She has become thinner; a year and a half ago she weighed 8 st., now she weighs a little over 6 st.

Present condition.—High complexion, skin and subcutaneous tissues of the cheeks feel tough, skin of the nose red and shiny, lips puckered, mouth can be opened to a limited extent only. Scarcity of fat all over the body. The skin of the hands is hard, shiny and difficult to pinch up; the fingers are short, podgy and swollen, and cyanosed at the proximal phalangeal joints; their move-

ments are limited and in the little fingers there are flexor contractures. The feet are flat, the joints are swollen and the toes and forepart of each foot are cyanosed. The elbows cannot be fully extended, the knees are prominent and rounded, and full extension is not possible at them.

No changes are present in the nervous, circulatory or respiratory systems.

(6) *A Case of Dermatomyositis.*

By Dr. MARTIN.

The symptoms had commenced gradually one and a half years before with pains in the limbs and swelling in the hands and feet. There had been no rise of temperature during the time the patient had been under observation. The most striking feature was the marked hardening of the skin and the subcutaneous tissues, and the presence of firm nodules scattered irregularly over the limbs; one of these was excised. At this operation there was found to be a marked thickening of the subcutaneous tissues. The nodule consisted merely of a fatty centre surrounded by a capsule of dense fibrous tissue, in which there were numerous inflammatory cells. In this case the limbs only were affected.

Dr. PARKES WEBER, in discussing the second case, pointed out that dermatomyositis is an acute inflammatory lesion of the muscles which has been frequently confused with trichinosis in countries where this disease exists. On examining this case he found no evidence of an inflammatory lesion of the muscles, while it appeared to him that the nodules were merely circumscribed lipomata. The condition is therefore not a dermato-myositis, but an affection closely allied to sclerodermia.

The first case seems to be one of typical generalized sclerodermia. It was interesting that so much improvement had been noticed, and he inquired as to the treatment which had been adopted.

The PRESIDENT drew attention to the curious course run by some of these cases, and to the fact that the muscles are sometimes involved. He recalled a case of acute sclerodermia, from the manifestations of which the patient had made a complete recovery, but then developed typical symptoms of progressive muscular atrophy.

Dr. MARTIN in replying stated that the second case had been treated by thyroid extract, sinusoidal current baths and massage during the past three months, and that it was under this treatment that some degree of recovery had taken place.

CLINICAL MEETING AT THE NATIONAL HOSPITAL FOR THE
PARALYSED AND EPILEPTIC, QUEEN SQUARE, W.C., ON
THURSDAY, JANUARY 11.

Dr. WILFRED HARRIS, President, in the Chair.

(1) *Case of Dystrophia Myotonica.*

By Dr. W. J. ADIE.

W. A., aged 44. Married. Enjoyed good health until March, 1917, when whilst undergoing military training he passed through a severe feverish illness diagnosed as influenza; during convalescence he suffered from severe pains in the lower limbs; the pains subsided in a few months but left behind them a weakness of the lower limbs which steadily increased, and soon appeared in the arms as well. About a year after the onset of weakness in the legs, and some time after the arms became weak, he noticed that he had difficulty in relaxing his grasp; this trouble persists. His facial appearance has altered considerably; all his muscles have wasted; his speech is not so clear as it used to be; his hair is falling out rapidly; he has lost over 2 st. in weight; he has not had sexual connection for some years and desire is absent. Apart from weakness in the limbs he feels well. He has never heard of a similar complaint or of cataract in any other member of his family. He has four healthy children.

Present condition: Facies myopathica; atrophy of sternomastoids, deep neck muscles, forearms and legs. Active myotonia in hand grasps. Reactive myotonia in tongue, small muscles of hands, deltoids and thighs. All tendon reflexes absent. Frontal baldness, acro-cyanosis, small soft testicles, narrow, high-arched palate.

(2) *Case of Myotonia Congenita.*

By Dr. LEWIS R. YEALLAND.

P. S., aged 18, male; one of twins. A paternal uncle suffers from cataract; nothing else from an hereditary point of view is discoverable. The patient was breast-fed and there was no difficulty in feeding him. He began to walk at the age of 2 years (a year later than his twin brother), was clumsy and made slow progress. At the age of 2½ his mother first noticed that when the patient's face was slapped for punishment, "his nose drew over to one side and remained there for a few seconds." At the age of 3, the patient was taken to India with his parents, and during his five years there nothing abnormal was observed; he walked normally and played games with other children. At the age of 8, he returned to England and began school. During his first week there (a) he saw double when looking at the blackboard from an angle; (b) his hand became "stiff" when writing and he was unable to release his pencil from it; (c) at the first school drill he was compelled to fall

out after twenty minutes' participation, on account of a gradually increasing stiffness which began in the neck and spread rapidly to the arms, trunk and legs. The stiffness was superseded by limpness, and in less than thirty seconds from the commencement of the symptoms he fell and was unable to move. He was taken home and remained in bed three days limp and helpless, but was able to swallow his food when fed. Similar attacks have occurred since during exertion, and an attack will come on after thirty minutes to one hour's walk in the cold. In warm weather he is almost free from the attacks. After prolonged rest the patient is much better, and he is in his best state the first thing in the morning after a prolonged rest. The condition is gradually becoming worse.

The patient is well developed. There are no deformities. Skin, mucous membrane, skull and spine, heart and lungs are all normal. The optic discs are clear and there are no evidences of organic changes in the central nervous system.

Repetition of any voluntary movement to order (e.g., eye movements, whistling, biting, yawning, flexion and extension of the elbow, wrist, knee or ankle) produces a gradually increasing tonic contraction of the part and will, if persevered in, result in complete cessation of movement. The same state of stiffness can be induced by the patient at will by throwing groups of muscles forcibly into contraction. Relaxation of muscles occurs gradually and is independent of the patient's will. Relaxation of the hand grasp is slow and awkward, the index finger extends first, followed by the others in succession, and the movement seems to be dependent on the patient's effort. A slow tonic contraction of muscles follows a sharp tap of the percussion hammer. The myotonic electrical reactions are positive.

DISCUSSION.

Dr. JAMES COLLIER considered that there was no doubt about the diagnosis of myotonia congenita in this case. It showed in a typical manner the effect of cold in increasing the tendency to myotonia, and resembled most reported cases in that the spasms were not decreased by exercise of the affected muscles.

The PRESIDENT asked Dr. Yealland if he had seen attacks in which the patient was helpless. Was it possible that these attacks were in any way similar to attacks of family periodic paralysis?

Dr. YEALLAND replied that he had not himself observed such attacks, but the evidence he had been able to collect tended against this suggestion.

(3, 4, 5) *Three Cases showing Retraction of the Eyelids.*

By Dr. JAMES COLLIER.

(3) *Case of Tumour affecting the Mid-Brain.*

The patient presents the following signs: Pronounced psychic impairment. Papilloedema. The pupils react very poorly to light, often the right pupil does not react to light at all. Retraction of both upper eyelids. Defective upward

movement of the eyes. Right facial weakness, especially on emotional movement. Absolute incontinence of urine. Slight weakness of the right side of the body, with extensor plantar reflex on that side.

(4) *Case of Mid-Brain Lesion.*

A. K. History: In October, 1921, the patient noticed shaking of the right hand; it passed off after about a fortnight. In February, 1922, the tremor returned: both the right arm and the right leg began to shake and she had double vision; her speech became slow and jerky.

Examination: Discs clear. Nystagmus: Vertical in right eye, oblique in left. Defective upper movement of both eyes; left eye turned slightly downwards and inwards. Ptosis of right upper lid; retraction of left upper lid with positive von Graefe's sign. Speech very ataxic. During speech there is a rhythmical upward and downward movement of the eyebrows and tremor of the head. There is a coarse tremor of the right hand. No loss of power in the limbs. No changes in the reflexes, except that the plantar reflex on the left side is doubtful.

(5) *Case of Disseminated Sclerosis with Retraction of the Eyelids.*

G. L., aged 41. Right leg began to drag seven years ago; since then symptoms have been steadily progressive, and consist of stiffness in both legs, spasms of lower limbs at night, precipitancy of micturition and incontinence.

Examination: Pupils equal; react normally. Nystagmus. Retracted lids, von Graefe's sign present. Slight intention tremor in hands; no ataxy or loss of power of upper limbs. Lower limbs very spastic, frequent flexion spasms.

Reflexes: Arm jerks all present; knee and ankle jerks exaggerated. Abdominal reflexes absent, plantar reflexes both extensor. Cerebrospinal fluid shows no abnormality.

(6) *Case of "Spondylose rhizomelique."*

By Dr. JAMES COLLIER.

The vertebral column is rigidly ankylosed throughout its length; the hip joints and knee-joints are also immobile; the right shoulder-joint shows great limitation of movement. The disease began ten years ago; patient has been in a spinal carriage for five years.

X-rays showed ossification of the short intervertebral ligaments.

DISCUSSION.

Dr. J. G. GREENFIELD asked whether there was in this case any sign of gonorrhœa, or of any focus of chronic sepsis. Some cases of this affection had been attributed by French writers to gonorrhœa. He remembered a case under Dr. Batten's care in the National Hospital in 1911,¹ in which gonorrhœa

¹ Case shown at Meeting of Neurological Section of the Royal Society of Medicine, May 4, 1911.

was suspected but could not be proved. In the majority of cases the disease commenced about the age of 20, and this fact, as well as the nature of the pathological changes and the distribution of the ankylosis (which always left the hands unaffected) distinguished spondylose rhizomélisque from the chronic rheumatic diseases of the spine.

Dr. COLLIER replied that of six cases of this condition which he had observed none had suffered from gonorrhœa, nor was there any history or evidence of it in the present case. In one of his cases the disease came on after puerperal sepsis, but in the others there was no focus of infection. In the majority of his cases the spine had been ventrally curved, but in one it was curved backwards as in the present case. In one case the affection started in the neck, and in six months spread down the spine to the sacrum rendering the patient as helpless as if he had developed total paraplegia. He considered that the ankylosis of the spine was never bony as there was always pain on any attempts at passive movement.

(7) *Case of Disseminated Sclerosis with Muscular Wasting.*

By Dr. JAMES TAYLOR, C.B.E.

H. C., aged 47. Previous health good. Fracture of left leg below knee when aged 13. Present trouble started eight years ago by the left knee giving way and the left leg becoming weak. One year ago he discovered that on reading he "was using the left eye only." About the same date the left grasp became weak and a sensation of pins and needles was felt in the left forearm and hand. There was also dysuria.

On admission, November 6, 1922: Vision of right eye $\frac{1}{15}$, of left $\frac{1}{20}$. Left disc distinctly pale, chiefly in temporal half. Nystagmus on lateral deviation to both sides. Marked spasticity of left upper and lower extremities. Wasting of left trapezius and muscles of left shoulder-girdle. Weakness of right rhomboids. The left arm and leg are less bulky and thinner than the right. Subjective sensation of pins and needles in left forearm and hand, and numb feeling in the feet. Slight diminution to cotton wool and pin-prick over left leg. Extensors wasted. Plantars, right extensor, left flexor. Left ankle clonus. Knee and ankle jerks increased. Abdominals absent left, doubtful right. Wassermann reaction negative in blood and cerebrospinal fluid. X-ray examination shows lipping and osteophytic outgrowths of cervical and lumbar vertebrae.

The evidence of disseminated sclerosis in this case rested chiefly on the nystagmus, the difficulty in articulation and the signs of lateral sclerosis. The winging of the scapulae was probably due to some other cause, and it was possible that the osteophytic growths in the spine might account for this and some of the other symptoms.

DISCUSSION.

Dr. COLLIER said that he would never admit wasting of muscles as a symptom of disseminated sclerosis.

The PRESIDENT said that he had seen quite definite atrophy of the interosseous muscles of the hands in disseminated sclerosis.

(8) *Case for Diagnosis: Spinal Compression or Disseminated Sclerosis.*

By Dr. F. M. R. WALSH.

E. W., aged 37. Past health good. Patient has six children, all in good health. Duration of symptoms eighteen months. Onset with pain in sole of left foot, followed by stiffness at back of left knee. In three months time lost the use of left leg. Sensation of pins and needles in left leg when it was accidentally bumped. The right leg became weak and powerless two months later. Dysuria for the last six months.

On examination, December 27, 1922: No abnormality of the cranial nerves or upper extremities. Legs usually in rigid extension, feet plantar flexed, halluces in extension. Marked adductor spasm. Flexor spasms of the legs have been becoming more frequent. No sensory changes. Knee and ankle jerks increased. Plantars give extensor responses. Abdominal reflexes: Upper feeble, lower absent. Reflex responses to cutaneous stimulation of both legs very active. Cerebrospinal fluid clear, colourless, no cells; total proteid 0.1 per cent. Wassermann reaction negative in blood and cerebrospinal fluid.

DISCUSSION.

Mr. C. P. SYMONDS said that he had never seen a case of disseminated sclerosis in which the protein in the cerebrospinal fluid rose as high as 0.1 per cent.

(9) *Case of Syringomyelia.*

By Dr. S. A. KINNIER WILSON.

L. H., aged 16. Previous health: Diphtheria, "rheumatism" at the age of 4, and frequently since in legs, arms, and shoulders. Operation for adenoids when 10 years old. Twelve months' history of painless sores on the right hand and fingers.

November 12, 1922: Experienced a feeling of coldness in right half of body. At the same time she noticed that she could not appreciate the temperature of water with the right arm or hand. At the same period she noticed the left pupil was getting smaller and the left eyelid drooping.

On admission, December, 1922: Left pupil smaller than right, left eyelid drooping. Slight impairment of tactile sensibility, marked thermal and pain loss in left trigeminal area. Tongue on protrusion deviates slightly to the left. Very slight spasticity of right arm and leg. Right leg weaker than left. Sensory loss to pinprick and temperature over right half of body up to a transverse line in mid-cervical region. Faint diminution to tactile stimuli over the same area. Knee and ankle jerks greater on right than on left side. Plantars: right doubtful, left flexor. Sphincters unaffected.

(10) *Case for Diagnosis, possibly Amyotonia Congenita.*

By Dr. S. A. KINNIER WILSON.

B. W., aged 11. Child born normally. Began to walk at normal age. He is the second youngest of eight children. At the age of 4 he was noticed

by his mother to be double-jointed. He began at this time to "fall about." The weakness of the legs has been progressive in the last three years. At present he is unable to stand unsupported.

Mentally the child is bright and intelligent. When sitting up the back is unduly rounded. The arms are thin and their strength poor. The muscular power of the legs is very poor. Impaired muscle tone in all limbs, the deficiency being greater in the legs than in the arms, over-extension at the knees on passive movements being very prominent. No contractures present. Arm-jerks very feeble. Abdominals active. Knee-jerks: Right greater than left, which is feeble. Ankle-jerks: Right feeble, left not obtained. Plantars: Right indefinite, left flexor. Sphincters unaffected.

(11, 12) *Congenital Neurosyphilis in Brother and Sister.*

By Dr. S. A. KINNIER WILSON.

(11) D. J., aged 10. Epileptiform fits since age of 5. Automatism, spitefulness. Mentally clear, Hutchinson's teeth. Pupils unequal, poor light reaction. Wassermann in blood, negative.

(12) G. J., aged 7. At the age of 5, paraplegia; unable to walk since arrest of mental development. Pupils Argyll-Robertson. Knee-jerks increased, plantars extensor, gait spastic and stamping. Ocular fundi, disseminated choroiditis. Wassermann in blood positive.

DISCUSSION.

Dr. JAMES TAYLOR said that in his experience two members of a family with congenital syphilis usually suffered in different ways. One of his patients, a boy who was afflicted with optic atrophy, was brought to hospital by a younger sister who had Hutchinsonian teeth, interstitial keratitis, and other signs of congenital syphilis, which were absent in the brother. The older patient eventually developed G.P.I. and died, whereas his sister remained free from symptoms of nervous disease.

The PRESIDENT said that Dr. Taylor's cases argued strongly against the assumption that there was a neurotoxic strain of the *Spirochæte pallida*.

(13) *Case of Syringomyelia, with much Sensory and Motor Impairment and little Wasting.*

By Dr. C. M. HINDS HOWELL.

M. G., aged 23. Patient "fell down" in a seizure or faint while at work in February, 1919. Afterwards she had an illness thought to be influenza. After the illness she was troubled with "hot sweats" affecting the left shoulder and left side of neck and head. Later she noticed weakness of the left hand while at work. In February, 1922, the right leg began to feel stiff and she had a sensation of cold waves passing up and down this limb.

On examination it is found that the left pupil is greater and the left palpe-

bral fissure smaller than on the right side. There is no nystagmus. There is partial loss of pain sense and of appreciation of cold over the left half of the forehead and over the lateral part of the left cheek. The left arm is weak, particularly the hand grasp; the thenar and hypothenar eminences are wasted. The deep reflexes are absent in the left arm. The right arm shows no weakness or wasting.

Both lower limbs are spastic, right more so than the left. The knee and ankle jerks are exaggerated and ankle clonus is present. Both plantar reflexes are extensor.

There is loss of tactile sensibility over the outer side of the right leg only. Pain sense is lost over both arms and both shoulders, and is impaired all down the right side of the trunk and over the whole of the right lower limb; on the left side of the body there is a similar impairment down to the lower border of the fourth dorsal segment both in front and behind.

Recognition of heat is completely lost over the whole of the right half of the body except the face, and over the left arm and left side of the trunk down to the level of the tenth dorsal segment. Loss of recognition of cold corresponds almost exactly in its distribution to the impairment of sensibility to pain.

(14) *Case for Diagnosis.*

By Dr. C. M. HINDS HOWELL.

G. S. In October, 1922, eight weeks before admission to hospital, patient's legs became weak while he was out walking; for about a week before that he had been losing the grip in the left hand and the left arm used to hang limply. Since the day when his legs gave way he has become steadily weaker and he has been aware of flickering in the muscles of his thighs. Since admission the right arm has become weak and he has become incontinent of urine and faeces. His neck has become stiff and it is painful when moved.

Examination: Left pupil slightly smaller than right. Fibrillation present in tongue. Complete flaccid palsy of left arm. Right arm becoming rapidly weaker. Abdominal and chest muscles weak; diaphragm does not seem to be acting. Left lower limb weaker than right. Fibrillation in muscles nearly all over the body, but especially in the thighs; wasting most pronounced in the muscles of the back and in the left lower limb. Sensory loss variable; fairly complete in both arms, less complete on chest with a level at the angle of the sternum. Sensory loss on the lower limbs much less than on the upper; right lower limb more affected than left. Reflexes: Knee-jerks brisk; plantars extensor.

Most of the signs presented by this case suggested the diagnosis of compression of the cervical region of the cord by a tumour. But this would not explain the fibrillation which was present. X-rays showed erosion of the second cervical vertebra and some shadows suggesting an intrathoracic tumour. As the condition was rapidly progressive he considered that it was

probably due to a diffuse sarcomatous or gliomatous invasion of the spinal cord. The cerebrospinal fluid contained 0.1 per cent. protein.

DISCUSSION.

The PRESIDENT described a somewhat similar case with total paralysis and anaesthesia of the right arm and partial paraplegia in which he had advised operation. The surgeon found no tumour, but noted no pulsations of the cord or dura mater. He therefore explored upwards under the laminal arches and came against a resistant mass. When he tried to break through this there was a gush of blood which proved, post mortem, to have come from an aneurysm of the posterior inferior cerebellar artery.

Dr. JAMES TAYLOR said that he had seen a similar case, which also presented the symptom of fibrillation of muscles, and which proved to be due to gliomatosis of the cord.

Dr. RIDDOCH described a case of quadriplégia with signs of spinal compression and multiple root lesions but with few sensory alterations, due to sarcomatosis of the meninges. The cerebrospinal fluid in this case was yellow, very highly albuminous and contained many tumour cells, some of which showed mitotic figures.

(15) *Case of Disseminated Sclerosis.*

By Dr. W. ALDREN-TURNER.

G. W., aged 35. About one and a half years ago patient began to be troubled with a trembling of the right arm, becoming more marked when he used the arm; this tremor has gradually become coarser. About the time the tremor commenced patient's gait became somewhat unsteady. Fifteen months ago his speech became jerky and has got steadily worse up to the present. Four years ago patient fell off a bicycle, striking his head and bruising his right elbow.

Examination: Discs normal. Pupils unequal, left greater than right, regular, slightly eccentric, some retraction of eyelids, react normally. External ocular movements good, no nystagmus, squint or diplopia. Movements of face, palate and tongue normal. Numbness in both hands. No demonstrable loss to pinprick or cotton wool. Sense of position in space and localization of touch normal. No astereognosis. Violent intention tremor of the right arm, so great that it shakes the whole body. The tremor is not purely intentional, for it is sometimes present mildly in the shoulder during rest. The left arm shows a slight tremor of the intention type. There is no loss of power or limitation of movement. Arm-jerks: equal on the two sides; biceps-jerk not obtained. Right knee and ankle jerks greater than left. No ankle clonus. Abdominals: present and equal on the two sides. Plantars: both flexor. Gross ataxia of gait: the arms, especially the right, make large movements which react on the whole body. No Rombergism. Wassermann reaction negative. The cerebrospinal fluid is normal except that it gives a "paretic" curve with the Lange test.

Progress: Little change noticed in arms, though patient feels that the tremor of the right arm now involves the shoulder more. Both legs are affected by tremor and the left is now rather worse than the right.

DISCUSSION.

Dr. SYMONDS said that he had noticed in the history of this case that the patient had had an illness called "influenza" six months before the onset of the tremor. He considered it possible that this was really a mild attack of encephalitis lethargica. He had seen involuntary movements follow an attack of encephalitis lethargica so mild as not to keep the patient in bed. He had observed Lange reactions of the "paretic" type in the cerebrospinal fluid of two cases of encephalitis lethargica.

Dr. RIDDOCH was inclined to agree with Dr. Symonds in considering that this case was due to encephalitis lethargica. The steady onset of symptoms without any remission was unlike disseminated sclerosis. He had often noticed similar gross involuntary movements come on gradually after encephalitis lethargica.

(16) *Case of Unilateral Affection of the 7, 9, 10, 11, and 12 Cranial Nerves.*

By Dr. C. P. SYMONDS.

Miss T., aged 30. In July, 1919, she had some teeth extracted. Shortly afterwards she noticed a discharge from her left ear, for which she did not consult a doctor. This was followed by gradually increasing deafness in the left ear. In March, 1920, she first noticed hoarseness which prevented her singing. About the same time she began to experience pain in the left shoulder and found that this occurred especially when she attempted to carry heavy objects in the left hand. In the summer of 1921 her voice improved, so that she was again able to recite, though singing was still impossible. The pain in the left shoulder was also less noticeable. During the last year the voice has again become hoarser, and the trouble in carrying things with the left arm has increased. She has also occasionally noticed some difficulty in swallowing. In October, 1922, for the first time she had a brief attack of left facial spasm. In this the eye closed and the whole side of the face was screwed up. Since then she has had several such attacks.

On examination the positive findings are: Left-sided conduction deafness, together with a fleshy mass obscuring the membrana tympani, probably a polyp. A fragment has been removed for microscopical examination, which shows it to be a capillary angioma. Left facial palsy of peripheral type. Paresis of the left vocal cord and left side of the palate. Weakness and wasting of the left sternomastoid and trapezius. Atrophic palsy of the left side of the tongue. Wassermann negative in blood. X-ray of head and upper cervical spine negative.

(17) *Case of Unilateral Affection of Cranial Nerves 9 to 12 (Tapia's Syndrome) associated with Chronic Otitis Media.*

By Dr. C. P. SYMONDS.

Miss C., aged 35. She has suffered from bilateral otorrhoea from time to time since childhood. She had tonsillitis at the age of 28, is subject to headaches, and has attended Guy's Hospital for constipation. In February, 1921, she first noticed hoarseness, and was referred from the medical to the throat department. It was there observed that the left vocal cord was paralysed. When seen a few days later the positive findings were: Paralysis of left vocal cord and weakness of left side of soft palate. Weakness and wasting of left sternomastoid and trapezius. Atrophic palsy of the left half of the tongue. Evidence of old-standing otitis media on both sides with a moderate degree of conduction deafness. The blood: Wassermann was negative. X-ray of the head and of the upper cervical spine showed no abnormality.

Under observation this patient has shown little change during the past two years except for the tendency of the hoarseness to diminish.

DISCUSSION (Cases 16 and 17).

The PRESIDENT considered Dr. Symonds's cases to be similar to those described in textbooks as "polyneuritis cranialis," the causation of which had been traced in some cases to otitis media.

Dr. COLLIER said that he had followed seven similar cases to autopsy, and in every case osteomyelitis of the base of the skull had been found. In one the disease had followed a bullet wound of the cranium; in another a tubercular osteomyelitis of the basi-sphenoid, and in the remainder ear disease was the cause. The appearance seen in the posterior fossa at autopsy was a plum-coloured cushion of raised and thickened dura mater with disintegration of the underlying bone. In every case the causative organism was a streptococcus. The long duration and the absence of pyrexia were remarkable. In one case there was no clinical evidence of otitis media, although the autopsy proved that this had existed. He placed no reliance on X-ray evidence in this condition, as it was very difficult to get satisfactory radiograms of the posterior cranial fossa. The cause of death in his cases had been lepto-meningitis in every case except the tubercular one, in which the carotid artery was eroded, and burst into the pharynx. One case had developed a hemiplegia, which was found to be due to thrombosis of the superficial veins of the brain. Replying to a question by Dr. SYMONDS whether the operative findings in Case 16 were not against his conception of the disease, Dr. COLLIER replied that in two cases following ear disease autopsy showed that the mastoid region was healthy, but that the infection had spread through the apex of the petrous bone.

NOTICES OF RECENT PUBLICATIONS.

Nerve Exhaustion. By MAURICE CRAIG, C.B.E., M.D., F.R.C.P.
Pp. 148. London: Churchill. 1922.

This small volume is intended as a guide to the treatment of nervous exhaustion, under which term the author includes a large number of morbid conditions, arising from many different causes; these are considered in detail. He treats very shortly of emotional shock, over-work, worry, and touches on physical states, such as puerperium and lactation, which lead to exhaustion. These various symptoms are attributed for the most part to "hypersensitivity," congenital or acquired, on which the author lays great stress. A chapter is devoted to sleeplessness, and the final section to treatment in general. The book is intended for the general practitioner, who is anxious to learn in simple language the means at his disposal for dealing with this aspect of the functional psychoneuroses.

Etudes Neurologiques. By GEORGES GUILLAIN. Pp. 469. Paris:
Masson et Cie. 1922. Price 25 francs.

The author has reprinted in this volume all those earlier papers in which he has brought forward any new facts related to the symptomatology and pathogenesis of nervous disorders. He has arranged them, not in chronological order, but in separate chapters according to the main subject with which they are concerned. The titles of these chapters reveal his wide interest and the valuable work he has done; the most important are: The fixation of poisons in the nervous system, pathology of the brain, pathology of the spinal cord, syphilis of the nervous system and tabes, muscular atrophies, changes in the cerebrospinal fluid, lethargic encephalitis and intoxications.

Many of the papers included are, it is true, only short communications originally published in various medical journals, and some perhaps are no longer of great interest or importance. But several of them at least have a real value, and the majority are certainly worth collecting together in a more permanent and easily accessible form. This is largely due to the fact that Guillain's interests have been mainly in the pathological and anatomical aspects of disease, and that his conclusions, as well as his hypotheses when he ventures on such, are solidly based on direct evidence of structural change. In fact in his introduction to this volume he insists that the anatomy and physiology of the nervous system must be the basis of any advance in knowledge which we can hope to attain, and that in the study of neuropathology all the modern methods of biology, bacteriology, chemistry and physics must be applied. A worker who has been guided by these principles must almost necessarily have valuable results to offer his readers.

Multiple Sclerosis (Disseminated Sclerosis): An Investigation by the Association for Research in Nervous and Mental Diseases. Pp. 241. New York: Hoeber, 1922.

The Second Annual Meeting of the American Association for Research in Nervous and Mental Diseases, which was held in New York in December, 1921, was devoted to a discussion on the etiology, pathology, symptomatology, differential diagnosis and treatment of disseminated sclerosis. The proceedings and conclusions of the commission are recorded in this volume, which constitutes a valuable contribution to our knowledge of this disease.

All the possible factors in the pathogenesis of the disease are discussed; several pages are even devoted to the hypothesis put forward by Jelliffe that as unconscious emotional factors are known to be under greater tension and more constantly operative than conscious ones which can produce somatic alterations, they may excite exudate phenomena in the blood-vessels of the nervous pathways intimately related to the function under repression, and therefore produce the characteristic lesions of disseminated sclerosis. But most of the papers and discussions are distinguished by a practical common sense. The sections on the vestibular and ocular manifestations of the disease are particularly interesting, and the negative results of Teague's prolonged research on its possible bacterial or protozoal origin are important in view of the recent repeated discoveries of causal micro-organisms. The chapters on the pathology of multiple sclerosis and on the changes that occur in the axis-cylinders are particularly complete.

The volume ends with a very comprehensive bibliography which, together with the statistical information collected in it, will prove extremely useful to all who wish to study the disease.

Der extrapyramidale Symptomenkomplex (das dystonische Syndrom) und seine Bedeutung in der Neurologie. By Professor G. STERTZ. S. 96. Berlin: S. Karger, 1921. Price 18 Marks.

This small monograph is devoted to those affections of the nervous system the most pronounced characteristics of which are disturbances in the functions of the motor system, and especially abnormalities of tone, unassociated with symptoms of affection of the cortico-spinal system. The clinical conditions included are progressive lenticular degeneration, pseudo-sclerosis, paralysis agitans, double athetosis, torsion spasm, spastic athetosis, choreic movements and myoclonia. In the second section the relations of the functional disturbances produced by non-systemic diseases of the basal ganglia, as arterio-sclerosis, disseminated sclerosis, tumour, encephalitis and poisons are considered; and the final chapter is devoted to a careful analysis of the pathology and physiology of the so-called extra-pyramidal systems. This is probably the section which will excite most interest, as subjects

claiming more and more importance in neurology are clearly and systematically dealt with in it. Unfortunately the author's style makes the reading of it difficult.

Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns. Teil 2, Lieferung 1. *Die Entwicklung der Zirbeldrüse.* von Professor F. HOCHSTETTER. S. 45 Mit 6 Abbildungen im Text unter 4 Tafeln. Wien und Leipzig: Deuticke, 1923. Price 10 Marks.

In this monograph, which is devoted to the development of the pineal gland in man and other mammals, Hochstetter has recommenced the issue of his valuable contributions to the embryology of the brain.

Certain features of disease of the pineal body have lately attracted considerable attention and consequently even to clinicians this monograph, in which many points on the origin and development of the gland are cleared up, offers some interest. It is, for instance, important that at one stage of growth the cells of its anterior lobe have an acinous or gland-like arrangement, suggesting a potential secretory function, which though not visible in the later stages of development may be reproduced in growths originating from these cells.

The plates by which the work is illustrated are extremely well reproduced, and make it possible to follow the descriptions of the text with ease.

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TO

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